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# **Risk factor analysis of diseases with public health importance in the Hungarian population, possibilities of prevention in primary care**

**PhD thesis**

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## **List of Abbreviations**

ACS: acute coronary syndrome

AMI: acute myocardial infarction

BMI: body mass index

BP: blood pressure

CKD: chronic kidney disease

CVD: cardiovascular disease

DM: diabetes mellitus

GFR: glomerular filtration rate

GOKVI: Gottsegen György National Cardiovascular Center

GP: general practitioner

HbA1c: glycated haemoglobin

HDL-C: high-density lipoprotein cholesterol

IDF: International Diabetes Federation

LDL-C: low density lipoprotein cholesterol

Mini-Cog: Cognitive Subscale

MKKK: Hungarian Cardiovascular Consensus Conference

MMSE: Mini–Mental State Examination

NCD: Non-communicable diseases

OECD: Organization for Economic Cooperation and Development

PAD: peripheral artery disease

REM: rapid eye movement

SBP: systolic blood pressure

SCORE: Systematic Coronary Risk Evaluation

TIA: transient ischaemic attack

WHO: World Health Organization

# 1. Introduction

Public health is a fundamental pillar of modern healthcare, with a focus on keeping people healthy and preventing diseases. To achieve these goals, identifying the risk factors of diseases and the opportunities for prevention are of paramount importance. Health management of the Hungarian population, like in other countries, faces many challenges. The efficient and effective organisation of healthcare, especially in primary care, is key to improving the health of the population.

The aim of this thesis is to comprehensively investigate the risk factors of some major public health disorders (cardiovascular diseases, dementia) in the Hungarian population and to present the prevention opportunities in primary care. In doing so, we aim to contribute to a better understanding of the health situation of population and to make recommendations for improving primary care and increasing the efficiency of the healthcare system.

## 1.1. Prevention

Prevention is a Latin term meaning the avoidance of a future unwanted event, which is a set of efforts to maintain and improve health, detect disease early, restore health in case of illness, and prevent disease progression.

The complexity of prevention can be understood by distinguishing its levels.

We distinguish three main levels:

1. *Primary prevention*: A set of activities aimed at maintaining health and preventing the onset of disease in case of people who do not yet show symptoms of the disease.

There are two main types of primary prevention:

- *Specific prevention*: interventions that target people at high risk or to protect against a particular disease. For example, vaccination against specific communicable diseases.
  - *Non-specific prevention*: interventions that aim to improve general health and thus reduce the risk of developing diseases. For example, anti-smoking programmes, and healthy lifestyle promotion, including healthy eating and physical activity.
2. *Secondary prevention*: the aim is to detect early the development of disease or conditions (risk conditions) in people who already have risk factors. These interventions are aimed at early diagnosis and treatment to prevent progression to later stages of the

disease. **Early detection - in real life - means screening and regular medical check-ups.**

3. *Tertiary prevention*: it aims to treat existing diseases and prevent their complications, to slow down disease progression and improving the quality of life in individuals already diagnosed. Examples are chronic disease management and rehabilitation (1).
4. *Kvaterner prevention*: aims to identify and avoid risks arising from healthcare, such as undue under-diagnosis, over-diagnosis, over-treatment and unnecessary prevention. Such excessive interventions can cause physical and psychological harm to patients (2).

Prevention is a priority for individuals, to reduce the health burden and increase the efficiency of healthcare systems.

## **1.2. Primary care**

Primary care has a long history in Hungary, with the first family doctors appearing in the late 19th century, during the Monarchy. The foundations of today's system of general practice were laid in 1992, when the system of general practice was legally declared, the scope of competence of general practitioners was defined and patients were given the freedom to choose their general practitioner (3,4). The primary care system of general practitioners is constantly changing but has always been the first line of defence for the health care system.

It ensures that individuals receive long-term, personalised, continuous health care in or near their place of residence, regardless of their gender, age or the nature of their illness (5).

„Primary health care covers the tasks of:

- the care for the prevention and early detection of disease;
- monitoring health status and providing health education, health promotion, and health planning support
- medical treatment, care and rehabilitation within the framework of a legally defined competence and in the context of a given diagnostic and therapeutic background;
- referral to a specialist for the diagnosis of illness, the preparation of a treatment plan or treatment;
- medical treatment, home care and rehabilitation, considering the therapeutic plan recommended by the specialist;
- care in the patient's home or a request for a specialist consultation in the patient's home.”

In light of the above, primary care is therefore involved at all levels of prevention, because of its accessibility, continuity and scope of competence covering a wide range of pathologies.

Countries with strong primary care systems have better health status of their citizens, lower rates of unnecessary hospital admissions and much lower socio-economic inequalities in access to health care (6).

### **1.2.1. Formation of cooperative communities of medical practices**

One of the cornerstones of the development of Hungarian primary health care is establishing a form of cooperation between medical practices.

In primary care, to improve patients' health status, the different professions (doctor, nurse, dietician, physiotherapist, health psychologist) work together in a community of practices, where they implement a preventive approach to patient care with a public health focus.

The first such community of practice initiative was implemented in the framework of the Swiss-Hungarian Cooperation Programme SH8/1 between 2012 and 2017, where twenty-four general practitioners' practices in sixteen municipalities and the patronesses of the districts concerned, together with new specialists, participated in the testing of the new primary care model, organised in 4 communities of practice. (7)

The programme aimed to raise health workers' awareness, expand primary care services with a preventive focus, address inequalities in access to care, and involve disadvantaged populations, focusing on the Roma population. Based on the Swiss Model Community of Practice methodology, with EU support, 45 communities of practice started operating in 2018 under the EFOP-1.8.2.-17 project and 6 in 2019 under the VEKOP-7.2.3.-17 project, covering 128 municipalities and serving nearly 600,000 people. The programme provided health assessments, individual and group physiotherapy, dietetics, and professional psychological services. The community practices could operate for at least 20 months and a maximum of 24 months (8).

The government initiated the "Three Generations for Health" programmes, rounds I and II, the third wave of community of practice initiatives. The programme was implemented between 2019 and 2021. In the first and second rounds, 79 and 64 consortia of GP practices were established, respectively, for a total of 143 consortia, covering almost 700 GP practices. The focus was on targeted screening and care activities for chronic diseases of public health importance. The strength of the programmes is their evidence-based clinical approach, which has enabled the procurement of targeted medical equipment, thus improving integration between primary and outpatient care.



### **1.3. Public health priority diseases**

From a public health perspective, priority diseases are diseases and health problems that significantly affect the population of a country or region and implies a serious public health risk. These priority diseases affect a large number of people, placing a significant burden on patients, their families and society as a whole.

The most important diseases of public health importance in developed countries today are non-communicable diseases. Non-communicable diseases (NCDs) - also known as chronic diseases - are among the leading causes of death, accounting for around 71% of all deaths each year, according to the World Health Organization (WHO). NCDs are health conditions that have a long course and slow progression, are non-communicable and are the result of multiple factors, including genetic, physiological, behavioural and environmental factors. The four most deadly non-communicable diseases worldwide are cardiovascular diseases (17.9 million deaths/year), cancers (9.3 million deaths/year), respiratory diseases (4.1 million deaths/year) and diabetes (2 million deaths/year)(9).

Cardiovascular diseases are the leading cause of adult morbidity and mortality in most of developed countries, and Hungary is in a worse position than the European Union average (10). The prevention of these diseases is, therefore, a public health priority, based on the timely identification and appropriate management of relevant risk factors.

As life expectancy increases, the health care of the elderly, in particular about vascular dementia, becomes an increasing challenge. Vascular dementia is a problem of increasing prevalence with major healthcare, social and economic implications. In 2017, the number of patients with dementia in Organisation for Economic Co-operation and Development (OECD) countries reached nearly 19 million. With ageing societies, in particular, due to the rising proportion of people over 80 years of age, and the lack of effective treatment, the OECD expects the number of people with dementia to rise to 41 million by 2050 (11).

In Hungary, experts estimate that between 250-300 thousand people live with dementia (12). Given the above, it is no coincidence that, in its report on chronic disease prevention, the WHO states that the therapeutic approach of healthcare systems must be replaced by prevention (13).

### **1.3.1. Cardiovascular diseases**

Cardiovascular diseases (CVD) is accounted for 38% of global deaths in 2021 (14).

More than three-quarters of CVD deaths occur in low- and middle-income countries. This may be due to inadequate access to primary health care programmes for early detection and treatment (14).

In Hungary, half of all deaths are caused by cardiovascular diseases (55% for women and 45% for men in 2022) (15).

#### **1.3.1.1. Risk factors for cardiovascular diseases**

Cardiovascular disease risk factors are physiological or laboratory abnormalities that indicate an abnormal condition; that increases the risk of developing cardiovascular disease in the population group in which they are present, compared to the population group without these factors. The recommendation of the Hungarian Cardiovascular Consensus Conference (MKKK), classifies cardiovascular risk factors into three groups: biologically determined, lifestyle-related and general risk factors (16).

##### **Biologically determined risk factors:**

###### **High blood pressure**

The prevalence and incidence of hypertension, a classic major risk factor, is steadily increasing. In Hungary, 40% of the adult population has hypertension, which increases with age, reaching 80% over the age of 75 (17,18).

###### **High blood sugar levels**

Type 2 diabetes mellitus is the most common form of diabetes, accounting for 90% of cases and 95% of cases over the age of 60. In Hungary, 14% of the adult population has been diagnosed with diabetes mellitus according to reports from general practitioners (17).

###### **Dyslipidemia**

A key risk factor for cardiovascular diseases. This includes elevated total and low-density lipoprotein (LDL) cholesterol levels, elevated triglyceride levels and reduced high-density lipoprotein (HDL) cholesterol. Every 1 mmol/l drop in LDL cholesterol level results in 22% lower cardiovascular mortality and morbidity (19,20).

More than 60% of the Hungarian adult population has elevated total cholesterol and 40% has elevated triglycerides. Although lifestyle has a significant influence on lipid levels, genetics also plays an important role in determining their serum amounts.

### **Overweight/obesity**

Overweight and obesity are important risk factors for cardiovascular diseases. Above the normal range (20-25 kg/m<sup>2</sup>), every 5 kg/m<sup>2</sup> increase in BMI (body mass index) increases the risk of developing cardiovascular disease by 40% (21).

In Hungary, 62.55% of the adult population, 53.2% of women and 71.9% of men are overweight or obese. The prevalence of overweight (BMI 25-30 kg/m<sup>2</sup>) is 44.6% for men and 29.9% for women, while the prevalence of obesity (BMI >30 kg/m<sup>2</sup>) is 27.3% for men and 23.3% for women (22).

According to the OECD report, considering BMI data, Hungary ranks fourth among OECD member states and first in Europe in obesity prevalence.

### **Metabolic syndrome**

According to the International Diabetes Federation (IDF) criteria set out in 2005, metabolic syndrome is defined as central obesity -(waist circumference  $\geq 94$  cm for men and  $\geq 80$  cm for women) and the presence of two of the following four factors (23).

- Elevated triglyceride concentration:  $>1.7$  mmol/l (or medication for this condition)
- low HDL cholesterol concentration:  $<1.0$  mmol/l for men,  $<1.3$  mmol/l for women (or medication for this condition)
- abnormal blood pressure:  $\geq 130$  mmHg systolic and/or  $\geq 85$  mmHg diastolic (or drug treatment for previously diagnosed hypertension)
- elevated fasting blood glucose concentration:  $\geq 5.6$  mmol/l or previously diagnosed type 2 diabetes

This group is continuously expanding with newly identified risk factors (e.g. adipokines, markers of chronic inflammatory status), but due to their limited practical applicability and lower predictive value, they are considered second-line risk factors.

## **Characteristics of lifestyle-related risk factors:**

### **Nutrition**

A healthy diet can reduce the relative risk of cardiovascular diseases by up to 30%.

Unhealthy diets, high in fat, sugar and salt, can contribute to obesity, high blood pressure and high total cholesterol. Low fruit and vegetable intake and inadequate intake of saturated and unsaturated fatty acids and trans fats are other important dietary characteristics (24).

### **Exercise**

Regular physical activity reduces the risk of developing the most common diseases: cardiovascular diseases, type 2 diabetes and malignancies. The WHO estimates that 4-5 million deaths worldwide could be avoided each year by an active lifestyle. The WHO recommends that at least 150 minutes of physical activity (walking, cycling, playing sports etc.) or 75 minutes of vigorous aerobic exercise per week are needed to achieve a positive physiological effect. In Hungary, 31.3% of adult men and 38.4% of adult women do not meet this recommendation, either at work or during leisure activities (25).

### **Smoking**

One of the oldest-known major risk factors for cardiovascular disease is smoking, which is accounted for by all risk estimation models. Approximately 1.3 billion people around the world smoke, 82% of whom live in low- and middle-income countries. In Hungary, 24.9% of the population aged 15 and over smoke daily. According to a 2019 survey, 31.1% of men and 28.7% of women aged 35-64 smoke daily (26).

### **Alcohol consumption**

The risk of developing cardiovascular disease can also be increased by drinking alcoholic beverages. The earlier theory of the preventive effect of low levels of alcohol consumption now seems to be being overturned. Recent research has shown that the lowest cardiovascular risk is associated with complete abstinence from alcohol (27).

In Hungary, according to the 2019 KSH data, 10% of men and 1.5% of women aged 15 and over declared themselves heavy drinkers (28).

## **General risk factors:**

### **Risk factors that cannot be influenced**

The risk of developing cardiovascular events increases with age. The male gender is associated with higher risk. The difference in risk between the two sexes begins to decrease in the age of 60s as estrogen levels decline in women.

When taking a family history, it is important to assess hereditary factors, which is an important part of the cardiovascular risk assessment process.

### **Risk factors can be influenced**

Education, income, living and working conditions also influence cardiovascular risk.

### **1.3.1.2. Cardiovascular risk assessment and risk classification**

Cardiovascular risk assessment as a method dates back to the 1970s. The first model of risk estimation was developed in the Framingham Study in the USA, which took into account: age, sex, blood pressure, smoking, total cholesterol or LDL cholesterol, HDL cholesterol, hypertension and diabetes mellitus (29).

In Europe, the first guideline was published in 1994 as the Joint European Task Force Recommendation, based on the results of the Framingham Study (30). The guideline provided clinicians with an easy-to-use risk chart, principles and practical options for risk reduction. In 1998, it was revised and the Second Joint European Task Force recommendation was published, using age, sex, smoking, systolic blood pressure, total cholesterol level and the presence of diabetes to estimate risk (31). The Third Joint European Task Force recommendation was published in 2003 (32). In contrast to the first two recommendations, this one is based on a European epidemiological database - distinguishing between low and high risk countries - and shows the probability of a fatal cardiovascular event over 10 years (not the probability of developing the cardiovascular disease) using the Systematic Coronary Risk Evaluation (SCORE) chart. A low risk is defined as a less than 2% risk of developing a lethal cardiovascular event within 10 years; a medium risk is defined as a risk of 2-4.9%; a high risk is defined as a probability of between 5-9.9%; and a very high risk is defined as a score of greater than or equal to 10%. As in previous recommendations, the SCORE also defines areas, targets and tools of intervention.

In 2016, the sixth Joint European Task Force Recommendation was published (20), which continued to build on the principles and the SCORE database from 2003, but with modifications to the current targets for intervention for each risk factor and the principles of drug prevention. It also provides an estimate of the probability of fatal cardiovascular events over the next 10 years.

- The SCORE chart is applicable between the ages of 40 and 65.
- It uses low, medium, high and very high-risk classifications.
- In this method, patients with a fatal cardiovascular risk of 5% or more are considered high risk.
- The parameters required for the calculation are age, sex, smoking, total cholesterol (or LDL cholesterol) level, and systolic blood pressure value.
- Relative risk can be determined individually based on the same age and parameters using a relative risk chart. It can be used to show how, for an individual of the same age, the risk value can be reduced by the modification of a risk factor (smoking, total cholesterol, blood pressure).

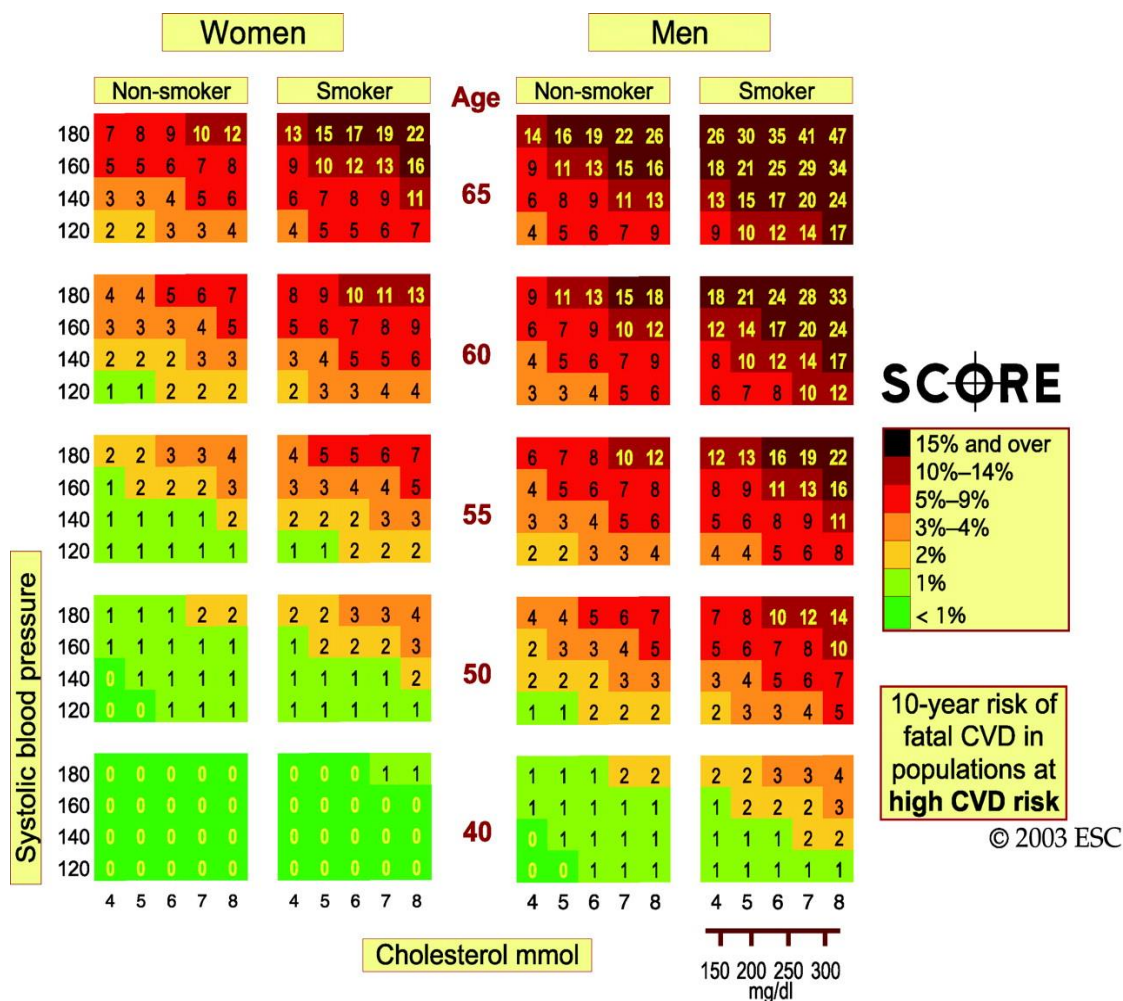


Figure 1. Ten year risk of fatal CVD in high risk regions of Europe by gender, age, systolic blood pressure, total cholesterol (33).

In 2021, the European Society of Cardiology published its latest guideline on this topic, which has changed radically compared to previous ones (34). It introduced a new risk estimation chart called SCORE2, which not only introduces changes in the parameters required for risk estimation (non-HDL cholesterol instead of the previous total or LDL cholesterol) but also extends its range from 65 years to 69 years and creates a chart for over 70 years (SCORE2-OP). Four geographic regions has been defined, based on which it classifies countries into separate risk groups; low, medium, high or very high risk, with Hungary being classified as a high CV risk region. It also takes into account the occurrence of non-fatal cardiovascular events, thus changing the percentage classification of risk categories, which are also given different cut-offs for different age groups (34).

Estimates the probability of fatal and non-fatal cardiovascular events over the next 10 years in apparently healthy patients (free of atherosclerotic disease, diabetes, chronic kidney disease, and extremely high cholesterol). Main characteristics of SCORE2 are as follows:

- The SCORE2 risk estimation table can be used between the ages of 40-69 years (SCORE2-OP can be used to estimate a similar risk in apparently healthy people over 70).
- It uses low-moderate, high and very high-risk categories.
- These risk classifications vary according to age (low-moderate risk: SCORE2 <2.5% under age 50; SCORE2 <5% between ages 50-69; high risk SCORE2 2.5-7.5% under age 50; SCORE2 5-10% between ages 50-69; very high-risk: SCORE2 >7.5% under age 50; SCORE2 >10% between ages 50-69;
- The parameters required for calculation are: region, sex, age, smoking, systolic blood pressure value, and non-HDL cholesterol level.
- It shows the potential for absolute risk reduction if a single modifiable risk factor is improved or eliminated. It can be used to show the increase in life expectancy for patients who appear healthy.



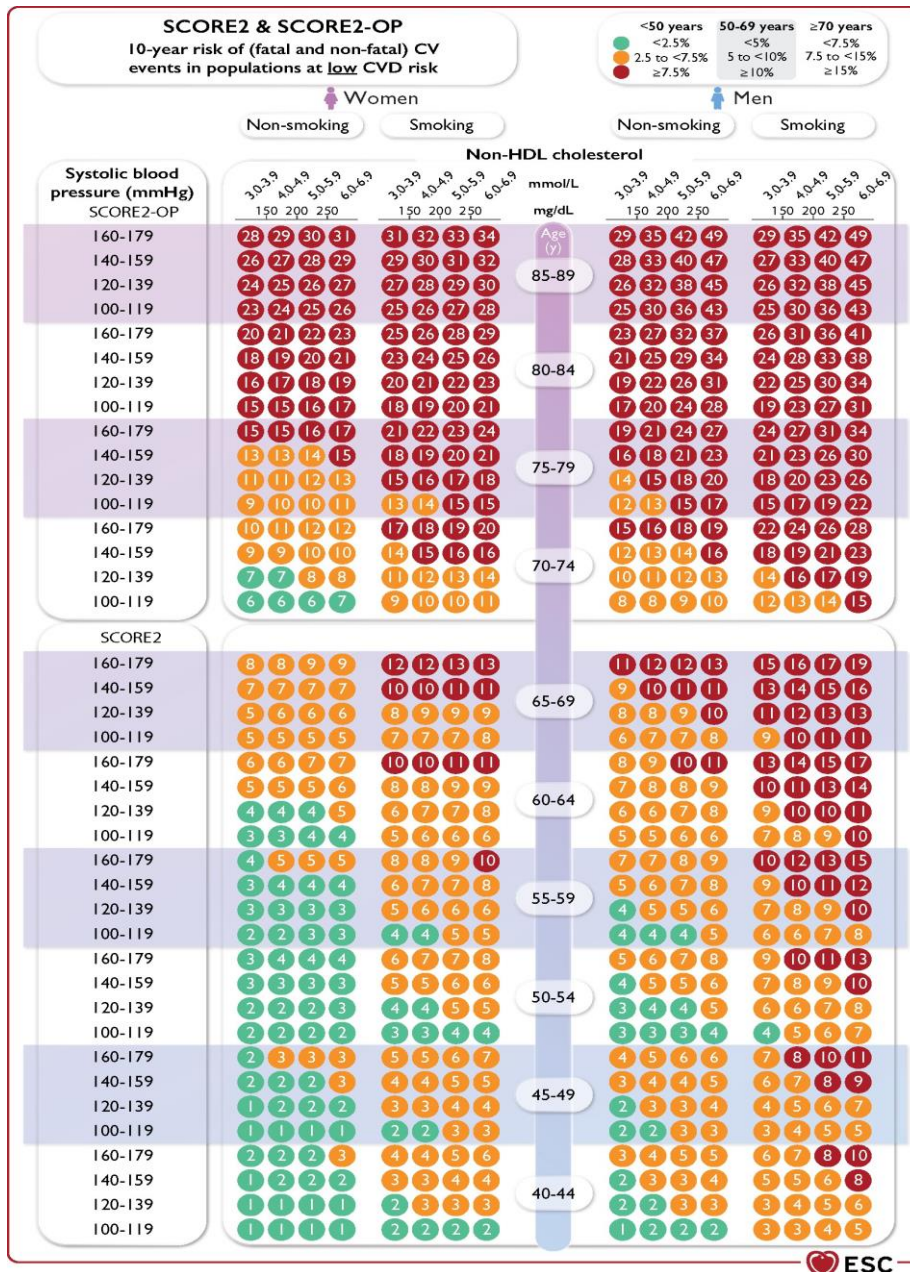


Figure 2. Systematic Coronary Risk Estimation 2 and Systematic Coronary Risk Estimation 2-Older Persons risk charts for fatal and non-fatal (myocardial infarction, stroke) cardiovascular disease (High-risk countries) (34).

To determine the overall cardiovascular risk, the SCORE table alone is not sufficient, as it considers a total of five or six classical risk factors. There are several conditions or other risk factors that, irrespective of the percentage estimated by SCORE, place a patient in a "high" or "very high" cardiovascular risk group.

Since 2003, the Hungarian Cardiovascular Consensus Conferences (MKKK) have been issuing recommendations on cardiovascular risk assessment, risk classification and intervention based

on the European guidelines, taking into account the preferences and practical additions of the Hungarian medical professionals (35).

At the start of the study presented here, the MKKK VII guideline was in force, so the recommendations for cardiovascular risk assessment were based on this guideline.

Patients should be classified as **very high-risk**, regardless of SCORE, if they: have experienced an acute major cardiovascular event (acute coronary syndrome, stroke or TIA (transient ischaemic attack), or critical limb ischaemia or revascularisation of these areas), or have clinically proven or documented coronary, cerebrovascular or peripheral atherosclerotic disease by imaging. Also included are patients with type 1 or type 2 diabetes mellitus who have a severe form of diabetes mellitus with target organ damage or a classical risk factor, severe chronic kidney disease with a GFR (glomerular filtration rate) below 30 ml/min/1.73m<sup>2</sup> and proteinuria. Patients with known and confirmed familial hypercholesterolaemia are also included.

A patient is considered **high risk** if they have: a blood pressure value above 180/110 mmHg, or a total cholesterol above 8.0 mmol/l, or a LDL cholesterol above 6.0 mmol/l, or an ankle-arm index  $\leq 0.9$ . Includes patients with type 1 or type 2 diabetes (excluding young type 1 diabetic) with no target organ damage or classical risk factors, chronic kidney disease with a GFR of 30-60 mL/min/1.73 m<sup>2</sup> and/or patients diagnosed with proteinuria.

One of the comprehensive studies which aimed the risk assessment and classification using the SCORE methodology described above is the EUROASPIRE (European Action on Secondary and Primary Prevention by Intervention to Reduce Events).

The EUROASPIRE IV study was conducted between 2012 and 2013 in 78 cardiology centers in 24 European countries. The study included 16 426 patients who had previously undergone myocardial infarction, acute coronary syndrome, or revascularisation (e.g., bypass surgery, angioplasty). The study evaluated patients' risk factor management, lifestyle habits, and drug therapy to assess the effectiveness of secondary prevention and the extent to which patients and physicians follow international guidelines (36).

The EUROASPIRE V study was the latest in the EUROASPIRE series, which ran between 2016 and 2017. The study aimed to identify persistent gaps in secondary prevention of cardiovascular disease, focusing on risk factor management and lifestyle changes. A total of 8 261 patients with a history of myocardial infarction, acute coronary syndrome, or revascularisation were enrolled in the study, which was conducted in 131 cardiology centers in 27 European countries. The study looked in particular at the effectiveness of treatment for

smoking, obesity, high blood pressure, high cholesterol, and diabetes and how well patients and doctors follow guidelines on prevention (37).

### **1.3.1.3. Prevention of cardiovascular diseases in primary care**

Given the increasing prevalence of cardiovascular disease, there is a growing need to focus on prevention, which is of particular importance in primary care because general practices have the potential to intervene at all levels of prevention.

At the level of primary prevention, it is important to emphasise health maintenance and prevention of risk factors, with the main focus on good nutrition, regular physical activity (30 minutes per day) and maintaining a normal body weight (BMI 20-25 kg/m<sup>2</sup>), avoiding smoking and alcohol consumption. In addition, about cardiovascular medication, it is important to manage risk factors to maintain target values (blood pressure <140/90 mm Hg, fasting blood glucose <6 mmol/l, total cholesterol <5 mmol/l).

At the level of secondary prevention, the aim is to detect an established disease or risk condition as early as possible and prevent a recurrence. At this level, the initiation of ACE inhibitor, beta-blocker and statin therapy is relevant (38).

The SCORE and SCORE2 visual charts are very important, as they allow the GP (general practitioner) to demonstrate the risk level of the patient based on the measured parameters, and to show how much the cardiovascular risk is reduced if a risk factor is changed (e.g. smoking cessation). Another important aspect is the promotion of regular screening.

At the level of tertiary prevention, the interventions to be implemented include supporting patients who have had a heart attack or stroke with medication, suggesting various rehabilitation programmes and referring them to specialists.

According to a US study, an increase of 1 GP per 10,000 people would reduce stroke mortality by 1.5% in one year and 3.6% in three years (39).

### **1.3.2. Dementia**

Dementia is an umbrella term for a group of symptoms that include memory impairment and disturbances in action, cognition and executive functions. Importantly, these symptoms/complaints disrupt daily life and indicate a deterioration of a previously higher cognitive state (40). The leading cause of disability and care dependency among people over 65; due to cognitive decline and the long course of the disease. The social and economic burden of the disease is enormous: during the long course of 10-15 years, the patient loses the ability

to care for himself/herself, requires supervision and then years of full-time care. According to a WHO report, by 2023, more than 55 million people worldwide will suffer from dementia, more than 60% of whom will live in low- and middle-income countries, with an estimated incidence of nearly 10 million. The number of people with dementia is projected to reach 82 million by 2030 and 152 million by 2050 (41). The OECD estimates that in 2018, 9.1 million people aged 60 and over in the European Union were affected by dementia. In Hungary, experts estimate that between 250 and 300 thousand people are living with dementia. If we want to quantify this at the level of families, the number of people affected, including their relatives, could exceed 1 million, which is 10% of the total Hungarian population (12).

In 2019, dementia related cost \$1.3 trillion worldwide, and around 50% of this cost is accounted for by informal caregivers (e.g. family members and close friends) who provide an average of 5 hours of care and supervision per day (41).

Dementia is currently the seventh leading cause of death and a major cause of disability and dependency among older people worldwide (41). Little is known about dementia in the public domain. The disease is often associated with stigma and exclusion - which can significantly delay the time to seek medical attention. Early diagnosis has many benefits for the patient and family, as well as for the care system. Professionals can offer patients a personalised life management or care plan, drug and non-pharmacological interventions. The role of general practitioners is prominent in both prevention and early diagnosis and care.

### **1.3.2.1. The main types of dementia**

#### **Primary degenerative dementias**

##### **Alzheimer's disease:**

Alzheimer's disease is the most common form of dementia and is associated with long-term progressive memory loss, cognitive decline and behavioural changes. It is characterised by neuronal necrosis and impaired communication between brain cells. The disease progressively worsens. It is the most common form of dementia and may play a role in 60-70% of all cases (42).

##### **Dementia with Lewy bodies:**

Involves the accumulation of small protein aggregates in the brain called Lewy bodies. It is characterised by a variable mental state that may include visual hallucinations, movement disorders, REM (rapid eye movement) sleep disturbances and distraction (43).

**Frontotemporal dementia:**

This form of dementia involves progressive lesions of the frontal and temporal lobes, which are involved in the regulation of emotions, behaviour and language.

Symptoms include changes in social behaviour, language difficulties and changes in emotions (44).

**Dementia associated with Parkinson's disease:**

As the disease worsens, mental decline may be associated with the main symptoms: slowing of voluntary movement initiation, decreased speed of movement, hand tremor at rest, and increased muscle tone (45).

**Huntington's disease:**

A congenital, paternally inherited, rapidly deteriorating degenerative disease of the central nervous system of unknown origin. Symptoms begin with behavioural disturbances, marked mental decline and specific movement disorders. The latter include muscle rigidity, muscle spasms, muscle twitching and, less frequently, involuntary spasmodic movements of the hands, feet, trunk and face (chorea). Other early symptoms may include difficulty speaking and unsteady gait (46).

**Vascular dementia:**

Vascular dementia is a consequence of cognitive and functional decline, stroke, blood supply problems or vascular stenosis caused by disease or injury to the vascular system of the brain. Vascular dementia is the second most common form of dementia after Alzheimer's disease, accounting for 10-25% of cases. Symptoms may vary depending on the areas affected by vascular catastrophes in the brain. In addition to cognitive decline, motor problems are often observed. It is characterised by a gradual onset and a staged course.

It is important to emphasise that for each type of dementia, individual symptoms and progression may vary and early diagnosis and appropriate treatment are of great importance in improving patients' quality of life and slowing down the progression of the disease. The individual treatment and care plan will depend on the type of dementia and the individual condition (46).

**Risk factors for dementia**

All factors that are also responsible for the development of atherosclerotic cardiovascular disease predispose to vascular dementia; older age; male gender; previous myocardial infarction, stroke, TIA; atherosclerosis; clot-forming diseases; high cholesterol; hypertension; diabetes; smoking; excessive alcohol consumption; obesity; and atrial fibrillation (46).

### **1.3.2.2. Screening for dementia**

#### **Mini-Cog Test**

The Mini-Cog (Cognitive Subscale ) test is a short cognitive assessment tool. It consists of two parts: a three-word memory test and a clock setting. The patient listens to three different words, (apple, chair and umbrella) and is then asked to draw an analogue clock and set the exact time (usually 10 minutes to three). The 3 words are then asked back. Each word recalled is worth 1 point, a correct clock test is worth 2, and an incorrect one is worth 0. Mini-Cog test scores 0-2, have a sensitivity of 39-84% and a specificity of 78-88% for mild cognitive impairment (47).

#### **Mini-Mental Test**

The Mini-Mental State Examination (MMSE) is a 30-item, quick-to-administer cognitive test used mainly to identify and assess the severity of dementia in medical practice. The test is not only important in assessing a condition but also in monitoring cognitive status over time, i.e. it can be used to follow a patient well.

The maximum score of the test is 30. Scores lower than this are interpreted according to predefined intervals. The areas of the test are orientation in space-time (10 points), immediate recall (recall memory 3 points), attention (5 points), delayed recall (recall memory 3 points), language skills (aphasia, alexia, agraphia) 5 points, praxis 3 points and visuospatial functions (1 point). The test takes 7-10 minutes. A cut-off score of 27-28 points in the MMSE test for the diagnosis of mild cognitive impairment implies a sensitivity of 45-60% and a specificity of 65-90%. For dementia, using the 23/24-point cut-off means 87% sensitivity and 82% specificity (48).

#### **Test Your Memory HUN**

Test Your Memory (TYM) is a 50-item short cognitive test that takes about 5 minutes to complete. It is a self-administered test and should be completed under the supervision of a healthcare professional. It consists of 10 tasks, including verbal fluency, sentence copying and

recall, semantic knowledge, counting, orientation, similarity recognition, naming, and spatial-visual ability. After validation in Hungary, the cut-off score for dementia is 35-36 points, with 94% sensitivity and 94% specificity (49).

### **1.3.2.3. Prevention of cognitive impairment in primary care**

Primary care for dementia can be complex and multifaceted, and is shaped by the needs of the individual, the progression of the condition and other factors. Primary care aims to support people and their families, provide the support and care they need, and improve their quality of life by facilitating their daily lives and activities. Regular access to medical and professional support is important to ensure that the best treatment methods are used and the best support is provided to individuals.

If the person (or a family member) with dementia presents symptoms to the GP, a diagnosis of the symptom complex can be made and, if necessary, a referral to a specialist (neurologist/psychiatrist). The GP is the main carer of a patient with dementia, both in terms of identifying and monitoring the disease and in terms of medication. It is important that acute hospital admissions are avoided and that, if hospital admission does occur, the patient stays in the hospital for as short a time as possible. The GP's work is carried out with a high level of professional knowledge, on an individual basis, with compassion, extending it to the patient's environment and considering the patient as an equal partner, based on the GP's list of competencies, partly in a definitive form and partly with the help of a specialist doctor, by professional recommendations. The level of severity of the dementia determines the level of care provided.

For vascular dementia, treatment focuses on the management of vascular disease and control of risk factors such as hypertension, and diabetes etc. Prevention also plays an important role here, particularly in terms of maintaining a healthy lifestyle, smoking cessation, regular exercise and a healthy diet. Treatment and support require individual therapy and care, taking into account the patient's condition and the severity of symptoms (40).

## **2. Objectives**

### **2.1. Differences of cardiovascular risk assessment in clinical practice using SCORE and SCORE2**

1. The primary objective of our study was to determine the cardiovascular risk level of the 40-65-year-olds involved in the “Three Generations for Health” programme using the 2016 European Guidelines on cardiovascular disease prevention in clinical practice (SCORE (Systematic COronary Risk Estimation)) on one side and the 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice (SCORE2) algorithms on the other side and to compare these results.

2. We also aimed to highlight the limitations of the routine use and interpretation of both methods in primary care.

### **2.2. Defining cardiovascular risk levels and assessing compliance with targets**

1. The second main objective of our study was to calculate the cardiovascular risk level, considering individual risk factors that determine cardiovascular risk, existing diseases that influence cardiovascular risk and family history, by the 2016 European guideline on clinical prevention of cardiovascular disease.

2. We also aimed to examine the success of reaching the target values for people at high and very high cardiovascular risk for certain risk parameters (blood pressure, lipid parameters, HbA1c (glycated haemoglobin), BMI, waist circumference), which is a good indicator of the effectiveness of cardiovascular risk management in primary and specialist care.

3. To place Hungarian risk management techniques in a broader international context, we also compared the effectiveness of attaining target levels in Hungary with results from other international surveys.

### **2.3. Assessment of cognitive impairment**

1. We aimed to describe the results of screening for cognitive decline in the target population over 55 years of age using the Mini-COG (Cognitive Subscale) and MMSE (Mini-Mental State Examination) tests, to describe the assessment of the results by the physician and to describe the subsequent fate of the patients.



### **3. Methods**

#### **3.1. „Three Generations for health" programme**

One of the most recent and comprehensive initiatives for cardiovascular risk assessment in Hungary, the "Three Generations for Health" programme was launched in 2019. The Government Decision 1234/2017 (28.04.2017) on Phase I of the Health Sector Policy Programme of the National Public Health Strategy for 2017 and 2018, point 1 c), specifies the implementation of a complex programme for the prevention of circulatory diseases as a task. (50)

The main objectives of the programme were to assess the risk factors for cardiovascular disease in the general population, to initiate individualised interventions, to improve patient cooperation in the care of patients who have had a heart attack or stroke and to monitor these activities. In addition to the cardiovascular focus, screening for fracture risk, dementia and atrial fibrillation in the age groups concerned was also part of the programme. The methodological activities of the programme were carried out under the leadership of the György Gottsegen National Cardiovascular Institute (GOKVI).

The Department of Prevention, Methodology and Organisation at GOKVI provided methodological support for the assessment of cardiovascular disease risk factors in general practices, monitoring of the programme, and provided IT support and training for the systemic operation of the programme. A further goal for the programme's roll-out is to increase the screening and subsequent intervention for lower limb arterial stenosis and to increase the social embeddedness of the programme.

The resulting data were processed in an online IT system (iCardio), which allowed for the centralised evaluation and analysis of data in an anonymous way and for the realisation of the research objectives.

All patients participating in the "Three Generations for Health" programme gave informed consent before taking part in the study. As the programme was launched under a Government Decision, the Council, in consultation with the Medical Research Council, considered that ethical approval was not required. All study methods complied with the relevant guidelines and standards.

In the first round of the programme, 453 general practitioners and general paediatricians started their professional programme in the first half of 2019 in 79 consortia. In the second round, 64 consortia were awarded grants, bringing the total number of participating practices to 353. In total, 806 practices from 143 consortia across the country participated in the programme by

completing their professional programme. A total of HUF 10.7 billion in funding was allocated to improve public health and prevention.

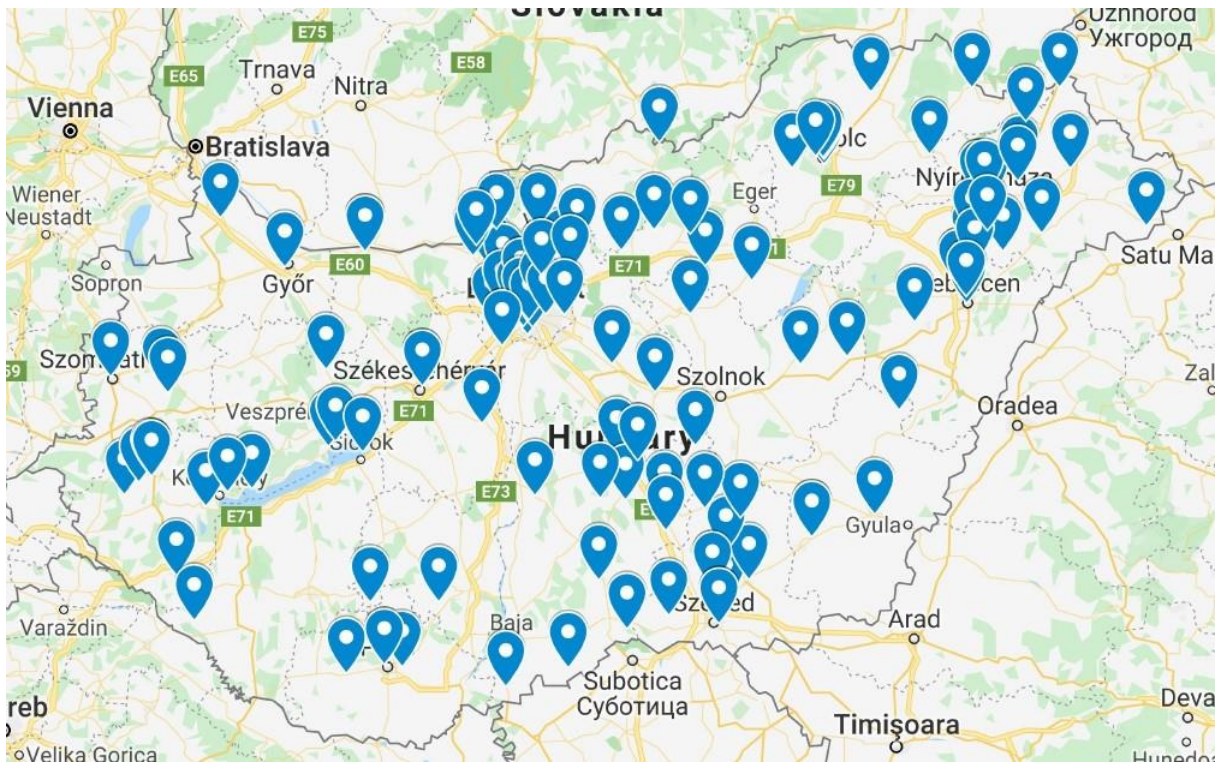


Figure 3. The location of the 143 consortia is shown on the map below (my own editing)

The focus of this study was to determine and compare cardiovascular disease risk levels using the two risk assessment methods, to assess compliance with target levels and to assess cognitive impairment.

### 3.2. Patients

Our study samples were patients aged 40-65 years (cardiovascular risk database) and over 55 years (dementia database), for whom electronic data were available, from GP practices participating in the “Three Generations for Health” programme.

Patients were recruited consecutively by attending a general practitioner's office in person or by telecommunication. Patients participating in the study signed a consent form. Participants' anamnestic data, parameters obtained during the physical examination performed on-site, and results of relevant laboratory tests were recorded in the general practitioners' offices. The laboratory measurements were performed in accredited laboratories (clinic, hospital or university), in each case in the facility serving the GP practice in daily clinical practice.

The data were provided via an online platform (iCardio), from where they were sent to the analysts in an anonymous, non-personally identifiable way. Naturally, each patient was given

a unique identifier in the system, which allowed his/her own GP to retrieve his/her data if necessary.

### 3.3. Differences of cardiovascular risk assessment in clinical practice using SCORE and SCORE2

Our data collection period was from January 1, 2019, to December 1, 2021. Our study sample consisted of patients aged 40-65 years who had all parameters available to calculate SCORE and SCORE2 values.

The parameters used to calculate the SCORE were age, sex, smoking status, total cholesterol (or LDL cholesterol) level, and systolic blood pressure value, which were calculated using the following equations:

$$\begin{aligned} S_0(\text{age}) &= \exp\{-(\exp(a)(\text{age} - 20)^p)\} \\ S_0(\text{age} + 10) &= \exp\{-(\exp(a)(\text{age} - 10)^p)\}^* \\ S_0(\text{age}) &= \exp\{-(\exp(a)(\text{age}-20)^p)\} \end{aligned} \quad \text{a).1.}$$

$$w = \beta_{\text{chol}}(\text{chol} - 6) + \beta_{\text{SBP}}(\text{SBP} - 120) + \beta_{\text{smoker}}(\text{current}) \quad \text{a).2.}$$

$$\begin{aligned} S(\text{age}) &= \{S_0(\text{age})\}^{\exp(w)} \\ S(\text{age} + 10) &= \{S_0(\text{age} + 10)\}^{\exp(w)} \end{aligned} \quad \text{a).3.}$$

$$S_{10}(\text{age}) = S(\text{age} + 10)/S(\text{age}) \quad \text{a).4.}$$

$$\text{Risk}_{10} = 1 - S_{10}(\text{age}) \quad \text{a).5.}$$

$$\text{CVDRisk}_{10}(\text{age}) = [\text{CHDRisk}(\text{age})] + [\text{Non} - \text{CHDRisk}(\text{age})] \quad \text{a).6.}$$

, where  $S$  is the underlying survival probability,  $\text{age}$  is the person's age now and for their age in ten years' time,  $\text{chol}$  is the cholesterol measured in mmol/L,  $\text{SBP}$  is the systolic blood pressure measured in mmHg,  $\text{smoker}$  is smoking coded as 1 for current and 0 for non-smoker,  $\text{CVD}$  is cardiovascular disease,  $\text{CHD}$  is coronary heart disease, and  $\text{Non-CHD}$  is non-coronary cardiovascular disease (33).

SCORE2 is calculated considering regional classification, sex, age, smoking status, non-HDL cholesterol level and systolic blood pressure.

The following sets of equations are required to calculate SCORE2:

$$r = 1 - e^{(-fatal\ rate)} \quad \text{b).1.}$$

$$S_{t+1} = S_t \times (1 - r_{cvd,t} - r_{comp,t}) \quad \text{b).2.}$$

$$CVrisk_t = \frac{r_{cvd,t}}{r_{cvd,t} + r_{comp,t}} * (S_t - S_{t+1}) \quad \text{b).3.}$$

$$CVrisk_{t1-10} = \sum_{1-10} CVrisk_t \quad \text{b).4.}$$

$$\frac{\text{Cumulative 10 year incidence total CV events}_{\text{without prior CVD}}}{\text{Cumulative 10 year incidence fatal CV events}_{\text{entire polulation}}} \quad \text{b).5.}$$

$$\begin{aligned} & CVDrisk_{total,10} \quad \text{b).6.} \\ & = \frac{\text{Cumulative incidence fatal + nonfatal CV events}_{\text{without prior CVD}}}{\text{Cumulative incidence fatal CV events}_{\text{General polulation}}} \end{aligned}$$

$$\begin{aligned} & \text{Calibrated 10 – year risk} \quad \text{b).7.} \\ & = 1 \\ & - \exp(-\exp(\text{scale1} \\ & + \text{scale2} \times \ln(-\ln(1 - un - \text{calibrated 10 – yr risk})))) \end{aligned}$$

,  $r$  is the 1–year mortality risks,  $S_t$  is the probability of being alive at start of interval  $t$ ,  $S_{t+1}$  is the probability of being alive at end of interval  $t$ ,  $r_{cvd,t}$  is the probabilities of experiencing a fatal CVD event, and  $r_{comp,t}$  is the competing event respectively during interval  $t$  (34).

After deconvolving the SCORE and SCORE2 algorithms, the calculated risk percentages were grouped according to the SCORE and SCORE2 category training, and then, for comparability, the SCORE small and medium categories were merged into a small-medium category to match the categories used in SCORE2, so that in both cases, small-medium, large and very large risk groups were created. In the application of SCORE2, the risk categories are different for each age group, so for ease of interpretation we have examined them separately.

### 3.4. Defining cardiovascular risk levels and assessing compliance with targets

Our study started in January 2019 and data were collected until 1 December 2020. Cardiovascular risk levels and targets were set according to the 2016 European guideline. In addition to individual data and family history (e.g. age, sex, smoking habits, chronic kidney disease, diabetes, early cardiovascular disease), certain vital parameters (blood pressure, BMI, abdominal circumference) and laboratory data (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, HbA1c) should be taken into account (20).

Table 1. The risk assessment methodology is summarised in the following table.

Categories of cardiovascular risk	Determining factors
Very high risk	<p>Subjects with any of the following:</p> <ul style="list-style-type: none"> <li>• Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI (acute myocardial infarction), ACS (acute coronary syndrome), coronary revascularisation or other arterial revascularisation procedures, stroke, TIA, aortic aneurysm, and PAD (peripheral artery disease). Unequivocally documented CVD on imaging includes plaque(s) on coronary angiography or carotid ultrasound.</li> <li>• DM (diabetes mellitus) with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension.</li> <li>• Severe CKD (chronic kidney disease) (GFR &lt; 30 ml/min/1.73 m<sup>2</sup>).</li> <li>• A calculated SCORE ≥ 10%.</li> </ul>
High risk	<p>Subjects with:</p> <ul style="list-style-type: none"> <li>• Markedly elevated single risk factors, especially serum total cholesterol &gt; 8 mmol/l (e.g., in familial hypercholesterolaemia) or BP (blood pressure) ≥ 180/110 mmHg.</li> <li>• Most other people with DM (except for young people with type 1 DM and without major risk factors who may be at low or moderate risk).</li> <li>• Moderate CKD (GFR 30–59 ml/min/1.73 m<sup>2</sup>).</li> <li>• A calculated SCORE ≥ 5 and &lt; 10%.</li> </ul>
Moderate risk	<ul style="list-style-type: none"> <li>• SCORE is ≥ 1 and &lt; 5% at 10 years.</li> </ul>
Low risk	<ul style="list-style-type: none"> <li>• SCORE &lt; 1%.</li> </ul>

The Hungarian cardiovascular prevention guidelines use minor changes for some targets, where relevant one risk factor was assessed according to both targets (35).

Table 2. Target values for risk factors in patients with high and very high cardiovascular risk

<b>Risk parameter</b>	<b>Target values for high-risk patients</b>	<b>Target values for very high-risk patients</b>
BMI	< 27 kg/m <sup>2</sup> (< 25 kg/m <sup>2</sup> )*	< 25 kg/m <sup>2</sup>
Waist circumference	men: < 102 cm, women: < 88 cm	men: < 94 cm, women: < 80 cm
Blood pressure	< 140/90 mmHg (diabetes: < 140/85 mmHg, nephropathy + proteinuria: < 130/80 mmHg)	< 140/90 mmHg (diabetes: < 140/85 mmHg, nephropathy + proteinuria: < 130/80 mmHg)
Total cholesterol	< 4.5 mmol/l	< 3.5 mmol/l
LDL-C	< 2.5 mmol/l (< 2.6 mmol/l)*	< 1.8 mmol/l
HDL-C	men: > 1.0 mmol/L, women: > 1.3 mmol/l (> 1.2 mmol/l)*	men: > 1.0 mmol/l, women: > 1.3 mmol/l (> 1.2 mmol/l)*
Triglycerides	< 1.7 mmol/l	< 1.7 mmol/l
HbA1c	< 7%	< 7%

\* target value according to the 2016 European Guidelines on cardiovascular disease prevention in clinical practice (35).

### 3.5. Assessment of cognitive impairment

Our study started on January 1, 2019, and our data had been collected until January 30, 2022. GPs participating in the programme first performed a mini-COG test on patients enrolled in the study, followed by the MMSE test if dementia was suspected, or the physician could choose to perform the MMSE test if the mini-COG was negative. A mini-COG result was considered abnormal if: 1) word recall was 1-2 points regardless of the clock test result, 2) the clock test was 0 points, 3) the clock test was negative but only 2 words were repeated successfully. In the case of word recall and the adequacy of the clock test, the suspicion of cognitive impairment was rejected. For the MMSE test, dementia was suspected if the score was 24 points or below. The scores obtained were grouped into the appropriate categories. In addition, the GP were also asked to classify the results (which appears in the tables as GP opinion). Overall, 79 827 patients in the community of practice were tested with mini-COG, and the result was 41 582 (52%) of patients were found to be free of abnormalities. In line with the objectives of the study, only those cases where mini-COG and MMSE test results were available, their assessment by the physician and data on referral to specialist care were analysed, so after a complete data cleaning, 29 730 cases were analysed.

### **3.6. Methodology for presenting results**

A cross-sectional study was conducted, where SCORE and SCORE2 were calculated based on the aforementioned algorithms, the calculated cardiovascular risk scores were - by gender-categorised into risk categories using the appropriate methodology. For comparability, the small and moderate cardiovascular risk categories defined by SCORE values were merged into a low-moderate category to match the category used in SCORE2. Thus, in both cases, we had 3 categories, which were the following: low-moderate, high and very high risk. For SCORE2, the percentage risk values were different for each age group, so to facilitate interpretation, we treated patients under 50 years and between 50-65 years separately. Therefore, the distribution of patients from the two age groups (<50; 50-65 years) were allocated by gender, with the two methods assigning different risk categories. Then, the distribution of the two algorithms that identify patients in the same risk category (by sex and age group) was shown using a cross-tabulation.

This was followed by the calculation of cardiovascular risk levels based on the 2016 European guidelines, then the proportion of patients reaching the target level stratified by sex and risk level was assessed. The proportion of patients at high and very high cardiovascular risk who were successful in reaching the target level was shown, and grouped by sex. The results of the target achievement values were compared with those reported by the EUROASPIRE IV and EUROASPIRE V trials.

Lastly, we examined the proportion of patients with suspected cognitive decline on the mini-COG and MMSE tests, by sex, age group and the opinion of the treating GP. We then showed the rates of referral to specialist care by sex, age group, mini-COG and MMSE test scores, and by GP assessment of test scores.

Data were presented with raw case numbers and the matching strata-proportions. Data were analysed using chi-square tests which could be considered as a powerful statistical method used to investigate the relationship between two categorical variables. The null hypothesis (H0) might have stated that there's no significant association between the variables, but the alternative hypothesis (H1) suggested there is a significant association. Whereas comparisons were made in the light of the observed frequencies of the data to the frequencies that would expect if there were no association between the variables. If the p-value given by the statistical test was less than the pre-defined chosen significance level (0.05), we rejected the null hypothesis and concluded that there was a significant association between the variables. If the chi-square test indicated a significant association, we elaborated on the nature of that association further. If not, we concluded that there was no evidence of a relationship between

the variables. For the analyses of these categorical variables SPSS 27 statistical software was used.



## 4. Results

### 4.1. Differences of cardiovascular risk assessment in clinical practice using SCORE and SCORE2

Our study included 85 802 patients aged 40-65 years, 35 172 (41.0%) men and 50 630 (59.0%) women. The mean age was 53.5 ( $\pm$ 6.75) years for men and 53.4 ( $\pm$ 6.81) years for women, with no significant difference between sexes ( $p=0.283$ ).

The age group under 50 included 27 453 people, of which 11 112 men (40.5%) and 16 341 women (59.5%). According to the SCORE calculation, 97.7% of men under 50 were classified as low-moderate risk, 2.1% as high-risk and only 19 (0.2%) as very high-risk. Based on the SCORE2 calculation, 32.4% of men were classified as low-moderate risk, 58.3% as high-risk and 9.3% as very high-risk. 100% of women under 50 fell into the low-moderate risk category based on the SCORE calculation Using the SCORE2 algorithm, 75.6% of women under 50 were low-moderate risk, 23.2% were high risk and 1.2% were very high-risk (table 3).

Table 3. Distribution of cardiovascular risk categories by sex under 50 years of age using SCORE and SCORE2 estimation

<50 age	Men		Women		Total	
	SCORE	SCORE2	SCORE	SCORE2	SCORE	SCORE2
<i>Low-moderate risk</i>	<b>97.7%</b> (n=10 853)	<b>32.4%</b> (n=3 599)	<b>100%</b> (n=16 341)	<b>75.6%</b> (n=12 345)	<b>99.0%</b> (n=27 194)	<b>58.1%</b> (n=15 944)
<i>High risk</i>	<b>2.1%</b> (n=240)	<b>58.3%</b> (n=6 479)	<b>0%</b> (n=0)	<b>23.2%</b> (n=3 784)	<b>0.9%</b> (n=240)	<b>37.4%</b> (n=10 263)
<i>Very high risk</i>	<b>0.2%</b> (n=19)	<b>9.3%</b> (n=1 034)	<b>0%</b> (n=0)	<b>1.2%</b> (n=212)	<b>0.1%</b> (n=19)	<b>4.5%</b> (n=1 246)
<i>Total</i>	<b>100%</b> (n=11 112)	<b>100%</b> (n=11 112)	<b>100%</b> (n=16 341)	<b>100%</b> (n=16 341)	<b>100%</b> (n=27 453)	<b>100%</b> (n=27 453)

In the 50-65 age group, 58 349 persons, 24 060 men (41.2%) and 34 289 women (58.8%) were analysed. 48.5% of men were classified as low to medium risk, 36.8% as high risk and 14.7% as very high risk using the SCORE estimation method. Using SCORE2 risk estimation, 24.2% of men were classified as low-moderate risk, 50% as high-risk and 25.8% as very high-risk. Using SCORE, 94.1% of women aged 50-65 years were classified as low-moderate risk, 5.4%

as high-risk and 0.5% as very high-risk. Using the SCORE2, 49.3% of the same patients were reclassified as low-moderate risk, 38.9% as high risk and 11.9% as very high risk (table 4).

Table 4. Distribution of cardiovascular risk categories by sex between 50-65 years of age using SCORE and SCORE2 estimation

<i>50-65 age</i>	<b>Men</b>		<b>Women</b>		<b>Total</b>	
	<b>SCORE</b>	<b>SCORE2</b>	<b>SCORE</b>	<b>SCORE2</b>	<b>SCORE</b>	<b>SCORE2</b>
<i>Low-moderate risk</i>	<b>48.5%</b> (n=11 668)	<b>24.2%</b> (n=5 831)	<b>94.1%</b> (n=32 260)	<b>49.3%</b> (n=16 892)	<b>75.3%</b> (n=43 928)	<b>38.9%</b> (n=22 723)
<i>High risk</i>	<b>36.8%</b> (n=8 843)	<b>50,0%</b> (n=12 024)	<b>5.4%</b> (n=1 867)	<b>38.8%</b> (n=13 318)	<b>18.3%</b> (n=10 710)	<b>43.4%</b> (n=25 342)
<i>Very high risk</i>	<b>14.7%</b> (n=3 549)	<b>25.8%</b> (n=6 205)	<b>0.5%</b> (n=162)	<b>11.9%</b> (n=4 079)	<b>6.4%</b> (n=3 711)	<b>17.6%</b> (n=10 284)
<i>Total</i>	<b>100%</b> (n=24 060)	<b>100%</b> (n=24 060)	<b>100%</b> (n=34 289)	<b>100%</b> (n=34 289)	<b>100%</b> (n=58 349)	<b>100%</b> (n=58 349)

The differences in the distribution of cardiovascular risk levels based on SCORE and SCORE2 are shown in Tables 5 and 6.

For men under 50 years of age (11 112 patients in total), 97.7% (n=10 853) were classified as low-moderate risk according to SCORE, whereas only 32.4% (n=3 596) of patients were classified as low-moderate risk using the SCORE2 algorithm. The remaining 58.2% of patients with a low to medium risk according to SCORE were reclassified as high risk and 7.2% as very high risk using SCORE2. 3 of men under 50 years of age were classified as high risk by SCORE and low-moderate risk by the SCORE2 formula.

In total, 3 633 people were identified as being the same by the two methods, i.e. placed in the same risk category, representing 32.7% of all men under 50 years of age in the study. However, using SCORE2, 7 257 persons, i.e. 65.3% of men under 50 years of age, were reclassified from the SCORE low-moderate risk category to the high or very high-risk category.

For women under 50 years of age, 75.6% of the population (n=12 345) can be classified as low-moderate risk using the SCORE and SCORE2 algorithms. No patients were placed in the high or very high-risk categories using SCORE. However, 23.2% of the women under 50 years of age who were identified as low-moderate risk by SCORE were identified as high risk by the SCORE2 formula, and 1.3% were identified as very high-risk. Overall 24.5% of women (n=3 996) were classified as in a higher risk category using SCORE2 (table 5).

Table 5. Distribution of cardiovascular risk categories comparing SCORE and SCORE2 by sex under 50 years of age

<50 age		Men				Women			
		SCORE2				SCORE2			
		Low-moderate risk	High risk	Very high risk	Total	Low-moderate risk	High risk	Very high risk	Total
SCORE	Low-moderate risk	32.4% (n=3 596)	58.1% (n=6 461)	7.2% (n=796)	97.7% (n=10 853)	75.6% (n=12 345)	23.2% (n=3 784)	1.3% (n=212)	100% (n=16 341)
	High risk	0.0% (n=3)	0.2% (n=18)	2.0% (n=219)	2.2% (n=240)	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)
	Very high risk	0% (n=0)	0% (n=0)	0.2% (n=19)	0.2% (n=19)	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)
	Total	32.4% (n=35 96)	58.3% (n=6 479)	9.3% (n=1 034)	100% (n=11 112)	75.6% (n=12 345)	23.2% (n=3 784)	100% (n=212)	100% (n=16 341)

Among men aged 50-65 years, 22.7% (n=5 452) of patients were classified as low-moderate risk, 23.0% (n=5 523) as high risk and 13.2% (n=3 165) as very high risk using both risk assessment methods. In total, 58.9% of men aged 50-65 years in the study, and 14 140 patients were identified as belonging to the same risk group by the two algorithms.

Based on the SCORE, 328 patients (1.4% of the total male population aged 50-65 years) were classified as high risk and reclassified as low-moderate risk using the SCORE2 formula. Of the men classified as very high cardiovascular risk by SCORE, 51 (0.2%) were reclassified as low-moderate risk and 333 (1.4%) as high-risk using the SCORE2 function. Using the SCORE method, 6 168 male patients aged 50-65 years (25.6% of all men aged 50-65 years) were reclassified as low-moderate risk and 48 (0.2%) as very high cardiovascular risk using the SCORE2 estimation method. The 2992 people (12.4%) in the high-risk category according to the SCORE are now in the very high-risk group according to the SCORE2. In total, 38.3% (9,208) of male patients aged 50-65 years are thus placed in a higher risk category using SCORE2.

Among women aged 50-65 years, the SCORE and SCORE2 cardiovascular risk estimates classified 16 876 women (49.2% of women aged 50-65 years) in the low-moderate risk group, 242 (0.7%) in the high-risk group and 155 (0.5%) in the very high-risk group.

For 0.1% of women (16) in this age group, the high-risk category calculated based on SCORE was changed to low-moderate risk using SCORE2. Of the group classified as very high risk

based on SCORE, 7 (less than 0.1% of the female patients aged 50-65 years studied) were moved to the high cardiovascular risk group.

Of the women aged 50-65 years in the low-moderate risk group based on SCORE, 38.1% were reclassified as high risk by the SCORE2 estimation and 6.8% were reclassified as very high risk. Of the women at high cardiovascular risk according to the SCORE algorithm, 1 609 (4.6% of women aged 50-65 years) were reclassified as very high risk by SCORE2. Thus, overall, 49.6% of women aged 50-65 years (n=16 993) were classified as being at higher cardiovascular risk when SCORE2 was used instead of SCORE.

Overall, 43.9% (n=37,673) of male and female patients aged 40-65 years in the study were placed in a higher risk category when using SCORE2 (table 6).

Table 6. Distribution of cardiovascular risk categories comparing SCORE and SCORE2 by sex between 50 and 65 years of age

50-65		Men				Women			
		SCORE2				SCORE2			
		Low-moderate risk	High risk	Very high risk	Total	Low-moderate risk	High risk	Very high risk	Total
SCORE	Low-mode rate risk	22.6% (n=5 452)	25.6% (n=6 168)	0.2% (n=48)	48.4% (n=11 668)	49.2% (n=16 876)	38.1% (n=13 069)	6.8% (n=2 315)	94.1% (n=32 260)
	High risk	1.4% (n=328)	23.0% (n=5 523)	12.4% (n=2 992)	36.8% (n=8 843)	0.1% (n=16)	0.7% (n=242)	4.6% (n=1 609)	5.4% (n=1 867)
	Very high risk	0.2% (n=51)	1.4% (n=333)	13.2% (n=3 165)	14.8% (n=3 549)	0% (n=0)	0.0% (n=7)	0.5% (n=155)	0.5% (n=162)
	Total	24.2% (n=5 831)	50.0% (n=12 024)	25.8% (n=6 205)	100% (n=24 060)	49.3% (n=16 892)	38.8% (n=13 318)	11.9% (n=4 079)	100% (n=34 289)

## 4.2. Defining cardiovascular risk levels and assessing compliance with targets

Our study included 37 778 patients aged 40-65 years, 14 944 (39.6%) men and 22 834 (60.4%) women. The mean age was 53.4 ( $\pm$ 6.95) years for men and 53.5 ( $\pm$ 7.03) years for women, with no significant difference in mean age between sexes (p=0.206).

Of our study population, 37 298 had all the information needed to determine their cardiovascular risk category. Using the 2016 European guidelines (20) for the prevention of cardiovascular disease 27.0% of patients had a low cardiovascular risk (women: 35.2%, men:

14.5%) (Table 4). 18.5% of the participants (men: 18.9%, women: 18.2%) were classified as medium risk, while 23.1% had a high cardiovascular risk (men: 27.1%, women: 20.5%). 31.4% of the participants had a very high cardiovascular risk (men: 39.6%, women: 26.1%). There was a significant difference ( $p < 0.001$ ) in the distribution of risk levels between the males and females.

Table 7 shows the distribution of cardiovascular risk levels by sex.

Table 7. Distribution of cardiovascular risk categories according to sex

<b>Risk factor</b>	<b>Men</b>	<b>Women</b>	<b>Total</b>
<b>Very high risk</b>	<b>39.6%</b> (n=5 843)	<b>26.1%</b> (n=5 885)	<b>31.4%</b> (n=11 728)
<b>High risk</b>	<b>27.1%</b> (n=3 995)	<b>20.5%</b> (n=4 615)	<b>23.1%</b> (n=8 610)
<b>Moderate</b>	<b>18.9%</b> (n=2 788)	<b>18.2%</b> (n=4 100)	<b>18.5%</b> (n=6 888)
<b>Low</b>	<b>14.5%</b> (n=2 144)	<b>35.2%</b> (n=7 928)	<b>27.0%</b> (n=10 072)
<b>Total</b>	<b>100%</b> (n=14 770)	<b>100%</b> (n=22 528)	<b>100%</b> (n=37 298)

#### *Achieving the target values in patients at high cardiovascular risk*

16.1% of patients (men: 18.6%, women: 14%) achieved a total cholesterol target of less than 4.5 mmol/l. The target LDL cholesterol level of less than 2.5 mmol/l was achieved by 16.8% of patients (men: 18.1%, women: 15.8%). 82.2% of patients at high cardiovascular risk (men: 90.3%, women: 75.1%) achieved the HDL cholesterol target level (men:  $>1.0$  mmol/l, women:  $>1.3$  mmol/l). 66.3% of patients achieved the target triglyceride level of less than 1.7 mmol/l (men: 61.5%, women: 70.5%).

A BMI target of less than 27 kg/m<sup>2</sup> was achieved by 48.5% of patients (men: 41.8%, women: 54.3%), and when the more stringent BMI of 25 kg/m<sup>2</sup> is considered, only 31.1% of our patients (men: 22.6%, women: 38.5%) achieved the target.

In terms of abdominal circumference, 44.4% of high-risk patients were on target (men:  $<102$  cm, women:  $<88$  cm), 55.1% of men and 35% of women achieved the desired abdominal circumference.

The target blood pressure (below 140/90 mmHg,  $<140/85$  mmHg in diabetes mellitus and  $<130/80$  mmHg in nephropathy+proteinuria) was achieved in 63.4% of patients in the high-risk

group (men: 56.8%, women: 69.1%). Among patients with type 2 diabetes mellitus, 57.3% achieved HgA1c below 7% (men: 51.6%, women: 63.2%) (table 8).

Table 8. Success in achieving target values in our study and in the EUROASPIRE IV study

High risk patients	“Three Generations for Health” Study			EURO ASPIRE IV
Risk factor and target value	Total	Men	Women	Total
<b>Total cholesterol:</b> <b>&lt; 4.5 mmol/l</b>	<b>16.1%</b> (n=1 388/8 610)	18.6% (n=744/3 995)	14.0% (n=644/4 615)	
<b>LDL-cholesterol:</b> <b>&lt; 2.5 mmol/l</b>	<b>16.8%</b> (n=1 426/8 478)	18.1% (n=707/ 3916)	15.8% (n=7 19/4 562)	18.4% (n=763/4 137)
<b>HDL-cholesterol:</b> <b>male: &gt; 1.0 mmol/l,</b> <b>female: &gt; 1.3 mmol/l</b>	<b>82.2%</b> (n=7 075/8 610)	90.3% (n=3 607/3 995)	75.1% (n=3 468/4 615)	
<b>Triglyceride:</b> <b>&lt; 1.7 mmol/l</b>	<b>66.3%</b> (n=5 710/8 610)	61.5% (n=2 455/3 995)	70.5% (n=3 255/4 615)	
<b>Blood pressure:</b> <b>&lt; 140/90 mmHg</b> <b>(diabetes:</b> <b>&lt; 140/85 mmHg.</b> <b>Nephropathy +</b> <b>proteinuria:</b> <b>&lt; 130/80 mmHg)</b>	<b>63.4%</b> (n=5 439/8 584)	56.8% (n=2 261/3 984)	69.1% (n=3 178/4 600)	44.7% (n=2 031/4 540)
<b>HbA1c &lt; 7% (patients</b> <b>with type 2 diabetes)</b>	<b>57.3%</b> (n=110/192)	51.6% (n=50/97)	63.2% (n=60/95)	58.5% (n=689/1 177)
<b>BMI &lt; 27 kg/m<sup>2</sup></b>	<b>48.5%</b> (n=4 155/8 570)	41.8% (n=1 665/3 980)	54.3% (n=2 490/4 590)	
<b>BMI &lt; 25 kg/m<sup>2</sup></b>	<b>31.1%</b> (n=2 667/8 570)	22.6% (n=899/3 980)	38.5% (n=1 768/4 590)	
<b>Waist circumference:</b> <b>(male: &lt; 102 cm,</b> <b>female: &lt; 88 cm)</b>	<b>44.4%</b> (n=3 378/7 606)	55.1% (n=1 957/3 549)	35.0% (n=1 421/4 057)	36.1% (n=1 585/4 392)

#### *Achieving the target in patients at very-high cardiovascular risk*

Only 4.7% of our patients in the very high cardiovascular risk group (6.1% of men; 3.3% of women) achieved a total cholesterol level below 3.5 mmol/l. The target LDL cholesterol level of less than 1.8 mmol/l was achieved by 8.0% of patients in this group (men: 9.5%; women: 6.5%). HDL cholesterol target (men: >1.0 mmol/l; women: >1.3 mmol/l) was achieved by 75.4% of our patients (men: 85.0%; women: 65.9%). Triglyceride targets below 1.7 mmol/l were reached in 55% of patients in the very high-risk category (men: 51.8%, women: 58.2%). A BMI target of less than 25 kg/m<sup>2</sup> was achieved by 17.4% of patients (men:15.0%, women:19.8%).

In terms of abdominal circumference, 14.3% of patients (<94 cm for men, <80 cm for women), 21.4% of men and 7.4% of women achieved the desired target, and a further 15.1% of patients

in the very high-risk group (men: 18.0%, women: 12.2%) achieved the more permissive abdominal circumference targets (men: 94-102 cm, women: 80-88 cm).

Nearly half (49.9%) of our patients at very high cardiovascular risk (men: 42.8%, women: 57.0%) achieved the target blood pressure (below 140/90 mmHg, <140/85 mmHg in diabetes mellitus and <130/80 mmHg in nephropathy+proteinuria). In patients with type 2 diabetes mellitus, achieving an HbA1c below 7% was successful in 53.0% (men: 50.3%, women: 55.8%) (table 9).

Table 9. Success in achieving target values in our own and in EUROASPIRE V

Very high-risk patients Risk factor and target value	“Three Generations for Health” Study			EURO ASPIRE V
	Total	Men	Women	Total (N=8261)
<b>Total cholesterol:</b> < 3.5 mmol/l	<b>4.7%</b> (n=550/11 728)	6.1% (n=355/5 843)	3.3% (n=195/5 885)	
<b>LDL-cholesterol:</b> < 1.8 mmol/l	<b>8.0%</b> (n=916/11 463)	9.5% (n=539/5 687)	6.5% (n=377/5 776)	29%
<b>HDL-cholesterol: male:</b> > 1.0 mmol/l. <b>female:</b> > 1.3 mmol/l	<b>75.4%</b> (n=8 842/11 728)	85.0% (n=4 964/5 843)	65.9% (n=3 878/5 885)	
<b>Triglyceride:</b> < 1.7 mmol/l	<b>55.0%</b> (n=6 450/11 728)	51.8% (n=3 025/5 843)	58.2% (n=3 425/5 885)	
<b>Blood pressure:</b> < 140/90 mmHg (diabetes: < 140/85 mmHg. nephropathy + proteinuria: < 130/80 mmHg)	<b>49.9%</b> (n=5 842/11 709)	42.8% (n=2 495/5 834)	57.0% (n=3 347/5 875)	58%
<b>HbA1c &lt; 7% (patients with type 2 diabetes)</b>	<b>53.0%</b> (n=2 217/4 183)	50.3% (n=1 066/2 121)	55.8% (n=1 151/2 062)	54% (n=29% of all patients)
<b>BMI &lt; 25 kg/m<sup>2</sup></b>	<b>17.4%</b> (n=2 038/11 698)	15.0% (n=876/5 829)	19.8% (n=1162/5 869)	18%
<b>Waist circumference (male: &lt; 102 cm. female: &lt; 88 cm)</b>	<b>29.4%</b> (n=3 166/10 784)	39.3% (n=2 104/5 348)	19.6% (n=1 062/5 436)	41%
<b>Waist circumference (male: &lt; 94 cm. female: &lt; 80 cm)</b>	<b>14.3%</b> (n = 1 543/10 784)	21.4% (n = 1 143/5 348)	7.4% (n = 400/5 436)	

### 4.3. Assessment of cognitive impairment

In our study, we analysed data from 29 730 individuals, 10 973 (36.9%) men and 18 757 (63.1%) women. The age group 55-64 included 9 356 (31.4%), the age group 65-74 included 11 879 (40.0%) and the age group 75 and over included 8 495 (28.6%) involved patients.

In the Mini-Cog test 3 515 people (11.8%) scored 0 and 5 112 (17.2% of the sample) scored 1. 4 266 (14.3%) scored 2 points and 6 255 (21.0%) scored 3 points, which meant that 64.4% of the study sample had a loss of at least 1 point, suggesting cognitive decline. The Mini-Cog test results showed that the prevalence of suspected cognitive decline was 55.6% (5 206 people) in the 55-64 age group. In the 65-74 age group, the prevalence was 64.0%, with 7 602 people affected. Among patients aged 75 years and over, the prevalence of the suspected disease was 74.6% (6 340 people). Misclassification was defined as cases where the GP did not interpret the score correctly. In 12 946 cases (44% of the patients studied), the GP did not consider the score abnormal, even though the results of the Mini-Cog test may suggest the suspicion of dementia. In 69 cases, the patients with the maximum score were classified as abnormal, which makes a total of 13 015 misclassified cases. 6 202 cases of cognitive decline based on Mini-Cog test scores and lesions considered abnormal by GPs were identical, representing 20.9% of the sample. There were 10 513 (35.4%) patients with the maximum Mini-Cog test score who were also classified by their GP as being in the normal range (Table 10).

Table 10. Descriptive analysis of the Mini-Cog test

		Mini-Cog		
		0-3	4	Total
Sexes	Men	63.1% (n=6 921)	36.9% (n=4 052)	10 973
	Women	65.2% (n=12 227)	34.8% (n=6 530)	18 757
Age group	55-64	55.6% (n=5 206)	44.4% (n=4 150)	9 356
	65-74	64.0% (n=7 602)	36.0% (n=4 277)	11 879
	75-X	74.6% (n=6 340)	25.4% (n=2 155)	8 495
GP opinion	abnormal	98.9% (n=6 202)	1.1% (n=69)	6 271
	normal	55.2% (n=12 946)	44.8% (n=10 513)	23 459
Total		64.4% (n=19 148)	35.6% (n=10 582)	29 730

The MMSE test results put 19 556 people in the normal range, which is 65.8% of our study sample. Mild dementia was found in 3 260 people (11.0%) and moderate dementia in 1 056 (3.6%). Severe dementia affected 5 858 people, representing 19.7% of the study population. Based on the test results, 3 725 men and 6 449 women were suspected of having dementia, with



a prevalence of 34.2% in both sexes. By age group, the prevalence was as follows: 2 469 people in the 55-64 age group were affected, with a prevalence of 26.4%, and 3 769 people in the 65-74 age group, with a prevalence of 31.7%. In the 75+ age group, 3,936 people, 46.3% of patients, were suspected of having dementia based on the results of the study.

Overall, the MMSE test showed that 34.2% of the total study sample (10 174 people) were suspected of having dementia. However, only 4 262 people (14.3% of the total sample) were declared to have abnormal test result by the GPs participating in the programme and 25 468 people (85.7% of the total sample) were considered that no abnormalities were found. Consistent with the MMSE test results, only 3 221 (31.7% of those with suspected dementia) were correctly identified by GPs as having a pathological condition, while 6 953 (68.3% of those with suspected dementia) were not identified as having a pathological condition, out of 10 174 patients with a score of 24 or below. Of the 4 262 patients assessed by doctors as having suspected dementia, 1 041 (24.4%) had normal test scores and were therefore incorrectly identified as having dementia (table 11.).

Table 11. Descriptive analysis of the MMSE

		<b>MMSE</b>		
		<b>0-24</b>	<b>25-30</b>	<b>Total</b>
<b>Sex</b>	<b>Men</b>	33.9% (n=3 725)	66.1% (n=7 248)	10 973
	<b>Women</b>	34.4% (n=6 449)	65.6% (n=12 308)	18 757
<b>Age group</b>	<b>55-64</b>	26.4% (n=2 469)	73.6% (n=6 887)	9 356
	<b>65-74</b>	31.7% (n=3 769)	68.3% (n=8 110)	11 879
	<b>75-X</b>	46.3% (n=3 936)	53.7% (n=4 559)	8 495
<b>GP opinion</b>	<b>abnormal</b>	75.6% (n=3 221)	24.4% (n=1 041)	4 262
	<b>normal</b>	27.3% (n=6 953)	72.7% (n=18 515)	25 468
<b>Total</b>		34.2% (n=10 174)	65.8% (n=19 556)	29 730

During the programme, GPs referred 2 233 people to specialist care, representing 7.5% of all participants. 10.9% of people with a Mini-Cog score (2 095) and 16.9% of patients with a Mini-Mental score (1 709) were referred to specialist care. Looking at the referrals based on GPs' assessment of the test results, 1 816 of the 6 271 people assessed by GPs as abnormal on the Mini-Cog test were referred to specialist care, representing 29.0% of those they assessed as

abnormal. 4 262 people had an abnormal score on the Mini-Mental test, of which 1 921 were referred to specialist care, representing 45.1% (table 12.)

Table 12. Referral to specialist care based on sex, age group, tests and doctor's opinion

		Referral sent to specialist care		
		Yes	No	Total
Sex	Men	6.4% (n=703)	93.6% (n=10 270)	10 973
	Women	8.2% (n=1 530)	91.8% (n=17 227)	18 757
Age group	55-64	3.4% (n=316)	96.6% (n=9 040)	93 56
	65-74	6.0% (n=714)	94.0% (n=11 165)	11 879
	75-X	14.2% (n=1 203)	85.8% (n=7 292)	8 495
Mini-Cog score	0-3	10.9% (n=2 095)	89.1% (n=17 053)	19 148
	4	1.3% (n=138)	98.7% (n=10 444)	10 582
Mini-Cog GP opinion	abnormal	29.0% (n=1 816)	71.0% (n=4 455)	6 271
	normal	1.8% (n=417)	98.2% (n=2 3042)	23 459
MMSE score	0-24	16.8% (n=1 709)	83.2% (n=8 465)	10 174
	25-30	2.7% (n=524)	97.3% (n=19 032)	19 556
MMSE GP opinion	abnormal	45.1% (n=1 921)	54.9% (n=2 341)	4 262
	normal	1.2% (n=312)	98.8% (n=25 156)	25 468
Total		7.5% (n=2 233)	92.5% (n=27 497)	29 730

## 5. Discussion

### 5.1. Differences of cardiovascular risk assessment in clinical practice using SCORE and SCORE2

Among men aged 40-50 years, the proportion of patients belonged to the low-moderate risk category decreased from 97% (based on SCORE) to 33% using the SCORE2 algorithm. This means that while just over 2% of patients were at high or very high-risk using SCORE, over 67% of the male population aged under 50 years were reclassified as at high or very high cardiovascular risk using the SCORE2 cardiovascular risk assessment method.

The 2021 ESC guideline, which introduces SCORE2, does not specify a 'mitigation' for meeting the blood pressure, lipid or HbA1c target values for high-risk and very high-risk patients, or even specify - a more stringent- 1.4 mmol/L LDL cholesterol target value for those at very high risk. Therefore, almost two-thirds of the male population aged 40–50 have a high-risk and very high-risk target when using the SCORE2 method compared with before, when this was required in just over 2% of patients (using the SCORE method). This means a radical increase in the number of patients needing care due to the higher level of calculated risk. It also increases the time and human resources required for care, which might imply increasing therapeutic costs.

For women under 50, the change in risk distribution between groups is not as radical, but still significant. Using the SCORE, 100% of this age group ~~were in~~ belonged to the low to medium risk category, while using the SCORE2 algorithm, 24% of our patients were reclassified as high or very high risk.

More than 75% of the male population aged 50-65 years were placed in the high or very high cardiovascular risk category using the SCORE2 risk assessment, compared to 51% of this population previously.

The most dramatic change occurred in our female patients aged 50-65 years. Using the SCORE algorithm, just under 6% of this population was in the high or very high-risk category, while using SCORE2 this proportion was over 50%.

In everyday clinical practice, the introduction of the SCORE2 means that more than 44% of the population aged 40-50 years (men and women combined) and almost 41% of patients aged 50-65 years will be moved to the high or very high cardiovascular risk category, instead of the previous low-moderate risk category.

This reclassification has implications for the achievement of the changed therapeutic targets and represents a very significant additional burden on the health care system, especially primary

care. The introduction of widespread use of SCORE2 is predicted to worsen the rate of target attainment, particularly for the LDL cholesterol target.

To the best of our knowledge, this thesis represents the first comprehensive comparison of SCORE and SCORE2.

## **5.2. Defining cardiovascular risk levels and assessing compliance with targets**

Among our patients at high cardiovascular risk, the prevalence of LDL cholesterol target attainment was 16.8%. This result is in line with the results of the EUROASPIRE IV study, which investigated LDL-C target below 2.5 mmol/l in 14 European countries and found that 18.4% of patients had this target.

Of the very high-risk patients, 8.0% achieved the LDL-C target of 1.8 mmol/l. This means that among our highest-risk patients, just under one in 12 patients achieved the lipid target.

For comparison, we used data from the EUROASPIRE V study, which was conducted in 27 European countries with more than 8000 participants. Our trial data show a significant lag compared to the success rate in European countries, where 29% of very high-risk patients achieved the LDL cholesterol target.

In our study, the success of attainment of HDL-C target was >80% in the high-risk group and >75% in the very high-risk group, with significantly better therapeutic efficacy in men than in women. Compared with a 2016 study in Hungary, HDL-C target attainment increased in both risk groups over the previous 4-5 years, from 66.7% to 82.2% in high-risk patients and from 68% to 75.4% in very high-risk patients (51).

When triglyceride levels were examined, we found that 66% of patients at high cardiovascular risk and 55% of those at very high risk achieved triglyceride levels below 1.7 mmol/l. In a 2016 study in Hungary, these rates were 47.8% and 45%, respectively, so there was some improvement in achieving the target for this parameter (51).

In our study, female patients achieved significantly better treatment results than male patients concerning triglycerides.

For blood pressure, 63.4% of high-risk patients and less than 50% of very high-risk patients in our study reached the target. Compared with the EUROASPIRE IV 2016 results, a more favourable target attainment was observed in our patients in the high cardiovascular risk group (63.4% vs 44.7%) (52). Among patients in the very high cardiovascular risk group, target attainment in our study was lower than the European data published in the EUROASPIRE V study in 2019 (49.9% vs 58%) (53).

The high-risk group achieved the BMI target (<27 kg/m<sup>2</sup>) with 48% success, compared with only 17.4% of patients in the very high-risk group, where the target was below 25 kg/m<sup>2</sup>. This

proportion is in line with European data from the EUROASPIRE V trial in 2019, where 18% of very high-risk patients had a BMI  $\leq$  25 kg/m<sup>2</sup> (37).

In our study, abdominal circumference target attainment among patients at high cardiovascular risk was 45% (women < 88 cm, men < 102 cm), compared with only 36.1% on average in the European countries included in the EUROASPIRE IV 2016 data (52).

In the very high-risk group, only 14% of our patients achieved the more stringent abdominal circumference target (women < 80 cm, men < 94 cm), with an extremely low success rate for our female patients (7.4%). Achievement of the more permissive (women < 88 cm, men < 102 cm) abdominal circumference target was more favourable, with 29.4% of our patients (women 19.6%, men 39.3%), but still significantly lower than the EUROASPIRE V results (41%).

HbA1c target achievement in high-risk patients with type 2 diabetes was 57.3%, which was not significantly different from the European average of 58.5% (43). 53% of patients with diabetes at very high cardiovascular risk had adequate HbA1c levels, which is close to the 54% target achievement reported in EUROASPIRE V. (53)

In everyday clinical practice, this means that Hungary is significantly behind the European average in achieving the targets for abdominal circumference and LDL cholesterol levels in patients at very high cardiovascular risk.

In the very high cardiovascular risk group, the achievement of the LDL cholesterol target (< 1.8 mmol/l) was extremely low (8%) compared to the European average (29%). This significant difference indicates a systemic problem.

The percentage of patients achieving the more permissive (< 102 cm for men and < 88 cm for women) abdominal circumference target was 29.4%, lower than the European average of 41%. The success rate for women in Hungary to reach the target abdominal circumference was particularly unfavourable (19.6%).

This suggests that the treatment/care of overweight and obese patients in Hungary is inadequate. Considering the role of abdominal obesity in increasing cardiovascular risk, improving the success rate of proper management and achievement of the target abdominal circumference is of paramount importance in reducing cardiovascular risk.

Non-pharmacological treatment and lifestyle modification are critical for the management of abdominal obesity, which requires complex patient support (e.g. nutritional therapy, exercise therapy, stress management), requiring a multidisciplinary approach and access to a wider range of specialists in primary care (54).

Our results show that the Hungarian healthcare system does not currently meet these criteria.

### **5.3. Assessment of cognitive impairment**

Dementia is an increasingly serious problem in developed countries, including Hungary.

The Dementia in Europe Yearbook 2019 estimates that by 2050, the number of people with cognitive impairment in Hungary will increase one and a half times due to a doubling of the population over 70 (55). This poses serious health, social and economic challenges. Early detection of cognitive decline has many benefits for both patients and carers. At the same time, current screening practices are not always professionally adequate and can have several drawbacks in the absence of adequate assessment.

Although tools for screening for cognitive impairment are available, detection of affected patients is often missed.

In the absence of sufficient evidence on the benefits and potential harms of screening (kvaterner prevention: inadequate diagnosis creates unnecessary anxiety and fear), mandatory screening at the population level has not yet been introduced. Instead, the practice of targeted screening of people presenting to GP practices with complaints of memory or other cognitive impairment has been adopted. Practices can use the miniCOG and MMSE tests to identify patients with suspected dementia.

Although the literature recommends measuring people aged 65 and over, our study sample was collected in the 55+ age group. Twenty-six percent of those in the 55-64 age group showed probable signs of cognitive impairment, and this prevalence increased in older age groups.

Even though a significant percentage of mini-COG and MMSE tests showed abnormal results, most of these results were misinterpreted (score-based classification and GP opinion were different) and only in one-third of cases was a referral made for specialist examination, contrary to the professional guidelines.

In primary care, half of GPs under-diagnose Alzheimer's disease or do not inform the patient of the diagnosis or suspicion (56).

Of course, communicating a suspected diagnosis is not an easy task because of the stigma and exclusion often associated with the disease, as well as concerns and legal issues.

However, in many cases, inadequate assessment of the results is due to a lack of knowledge. A survey of general practitioners in Hungary found that 80% of GPs had not received any training on dementia and felt helpless to treat patients (57). There is also a practice among GPs known as "watchful waiting": instead of referring the patient with dementia to specialist care promptly, GPs prefer to just instead of referring the patient to a specialist unit, they tend to observe the patient for a while, thus missing the opportunity for early treatment (58). Members of the older population were referred to specialist care at a higher rate, which may be due to the medical

perception of dementia as an elderly disease (59). Failure of referring to a specialist may be due to a lack of knowledge, professional uncertainty or inappropriate attitudes and practices. One of the drawbacks of population screening for dementia is that an inadequate diagnosis can create unnecessary anxiety and fear. The practice of family doctors in our study was adequate, as negative results were interpreted well and these patients were not referred to specialist care.

## 6. Conclusions

Based on our results, 43.91% of the cardiovascular risk screening population (37 673 patients) were considered to be at higher risk when using the SCORE2 method compared to the results obtained when using the SCORE method. This represents a radical increase in the number of patients at high or very high cardiovascular risk. This increased number of patients requires more time, more human resources (involvement of other interdisciplinary specialists: dieticians, physiotherapists, pharmacists, etc.) and increased therapeutic costs to achieve the more stringent therapeutic targets for patients.

This workload appears unmanageable in the current primary healthcare system and implies the need for new care modalities and operational structures.

Our database on the success of cardiovascular target achievement shows that most of our patients in the high and very high cardiovascular category are not achieving their outcome targets adequately and in many cases are significantly below the European average (EUROASPIRE IV, EUROASPIRE V).

These findings highlight the role of central obesity in the development of cardiovascular risk and the very low effectiveness of obesity therapy in Europe and in Hungary. To be successful in achieving the goals of reducing abdominal obesity and LDL-C, priority should be given to multidisciplinary teams (e.g. exercise therapists, nutritional therapists and health psychologists) that can provide appropriate support for lifestyle modification in these patients. Ideally, these teams would work in partnership within the GP practice.

Our dementia screening is the first study to widely assess the practice of detecting cognitive decline in primary care in our country. Practice groups used the accepted tools to screen for dementia, but the assessment of results and referral of suspected dementia cases to specialist care fell below the expected level.

There are several reasons for this shortfall, including ageing GPs, lack of knowledge, unfilled practices, high caseloads, disproportionate administrative tasks, burn-out syndrome and GPs attitudes toward dementia. There is a need to increase information in GP practices on the identification and management of dementia and to strengthen links with specialist care.

Additionally, the introduction of other dementia screening tests should be considered.

GP work is of particular importance at all three levels of prevention.

Initiatives to prevent cardiovascular disease and health education are essential, and the use of a cardiovascular risk calculator is key.



The organisation of screening programmes for the general public is of paramount importance for secondary prevention. There is currently no evidence of the effectiveness of a screening programme for cognitive decline. For both diseases, early diagnosis means therapeutic, life management and quality of life for the patient, processing, preparation, cooperation and care organisation for the carer, and effective, high quality professional work and patient satisfaction for the doctor.

The improvement of morbidity and mortality rates can also be achieved by improving diagnostic methods, drug therapies, the development of a multidisciplinary team of non-medical health professionals and the accessibility of health care. Improving these indicators would reduce the burden on society.

Countries with robust primary care systems, especially those that prioritize preventive care, consistently see better health outcomes for their citizens. Prevention plays a crucial role in reducing the incidence of chronic diseases, such as diabetes, cardiovascular disease, by identifying risk factors early and promoting healthy behaviors. As a result, these nations not only experience lower rates of unnecessary hospital admissions, but they also benefit from a more sustainable healthcare system that can focus resources on those who truly need intensive care.

Furthermore, preventive care contributes to significant cost savings in the healthcare system. By addressing health issues early through screenings, vaccinations, and lifestyle interventions, the need for expensive treatments and hospital stays is reduced. This proactive approach also minimizes the burden on emergency services and specialty care, allowing these resources to be allocated more effectively.

Another critical benefit of strong primary and preventive care is the reduction of socio-economic inequalities in healthcare access. In countries with well-developed preventive care systems, healthcare is more accessible to all segments of the population, regardless of income or social status. This leads to a more equitable distribution of health services, ensuring that vulnerable groups receive the care they need before health problems become severe. Consequently, there is a marked decrease in health disparities among different socio-economic groups, contributing to overall societal well-being.

Moreover, the emphasis on prevention and primary care fosters a culture of health literacy and empowerment among the population. Individuals become more knowledgeable about their health and are more likely to engage in self-care practices, adhere to medical advice, and make informed decisions about their well-being. This, in turn, leads to a healthier, more resilient population that is better equipped to manage its health over the long term.

In summary, countries with strong primary care and preventive health systems enjoy better health outcomes, lower healthcare costs, reduced strain on hospital services, and a more equitable and accessible healthcare environment. The focus on prevention not only enhances individual health but also contributes to the sustainability and efficiency of the entire healthcare system.

### **Study Limitations:**

One general limitation of our study is that patient recruitment was carried out using a consecutive method in general practices rather than through randomization. Moreover, our study was descriptive and cross-sectional, which limited our ability to establish cause-and-effect relationships.

A specific limitation of our SCORE and SCORE2 comparison is that this study analysed data from Hungary which belongs to a high-risk region.

Regarding cardiovascular risk analysis our results might be influenced by the fact that the study focused on a population from GP practices where the physicians may have been more motivated and committed to cardiovascular prevention. This is because participation in the study was voluntary for GPs and required extra effort beyond their usual daily activities.

### **Strengths of the study:**

A general strength of our study is that the number of patients reached is exceptionally high. A total of 806 GP practices from all over the country took part, which is more than 19% of the active adult and mixed practices.

A distinct advantage of our comparison between SCORE and SCORE2 to the best of our knowledge, we first compared the two cardiovascular algorithms.

A key strength of our cardiovascular risk study lies in the identification of the gaps in cardiovascular risk management in Hungary, particularly when compared to the European average. Our findings underscore the challenges in managing obesity, highlighting the critical need for improved strategies. The study suggests that general practice partnerships could play a pivotal role in driving positive changes in these areas.

Moreover, by screening for cognitive impairment in primary health care, our study is unique in our country.

## 7. Summary

Cardiovascular diseases are high on the mortality statistics and the prevalence of dementia is a growing challenge in the care of the elderly.

A cross-sectional survey was carried out among patients aged 40-65 years and 55 years and over, for whom electronic data were available, from GP practices participating in the “Three Generations for Health” programme. We collected data from 1 January 2019 to 31 January 2022. In our study, we compared cardiovascular risk levels for the population aged 40-65 years using the SCORE and SCORE2 algorithms and examined cardiovascular risk levels and attainment of targets based on the 2016 European guideline. For patients aged 55 years and older, we performed a mini-COG test, followed by an MMSE test for patients with suspected dementia.

In calculation cardiovascular risk, using SCORE, 97.7% of men aged 40–50 were low to moderate risk, decreasing to 32.4% with SCORE2. Among men aged 50–65, 36.8% were high risk and 14.8% very high risk with SCORE, while 50% were high risk and 25.8% very high risk with SCORE2. For women aged 50–65, using SCORE, 5.4% were high risk and 0.5% very high risk, compared to 38.8% high risk and 11.9% very high risk with SCORE2.

Among very high cardiovascular risk patients, only 8.0% reached the LDL-C target of 1.8 mmol/L, significantly below the European average. High-risk patients generally achieved better target blood pressure levels compared to the European average, but attainment was slightly lower in very high-risk patients. In our study, 29.4% of very high-risk patients achieved the abdominal circumference target, below the European average.

Cognitive decline was suspected in 64% of our patients using the Mini-Cog test and 34% using the MMSE test. Participating GPs considered 4262 patients to have abnormal results. Referral to specialist care was made for 11% of people with abnormal Mini-Cog test scores and 17% of people with suspected dementia based on MMSE test scores.

With the application of the SCORE2 algorithm, 43.91% of the entire population transitioned to higher cardiovascular risk categories, signifying a radical increase in the number of patients requiring care, especially burdensome for already overwhelmed primary care practices. In Hungary, the success rate of cardiovascular risk management is lower than the European average across several parameters. The practice of detecting cognitive decline and directing suspected cases to specialist care shows similar trends.

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