

# Hypertension treatment simply and effectively

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# Definition of arterial hypertension

**The most often disease of cardiovascular system**

**AH + hyperlipidemia +DM + nicotine addiction**

**premature atherosclerosis & ischemic heart disease**

- **Definition : repeated increase of blood pressure (systolic-diastolic) 140/90 mmHg or higher in patients older than 18 years in at least two of three measurements in two different checks**
- **In most cases it is a stable, sustained hypertension, may occur paroxysmal hypertension**

# Treatment goals in hypertension patients

## 2013 ESH/ESC - AH Treatment Management Guidelines

### **SBP < 140 mm Hg**

patients with low and medium CV risk  
patients with diabetes mellitus  
prior stroke or ischemic attack  
ischemic heart disease  
chronic kidney disease

### **SBP between 140 to 150 mm Hg**

older patients < 80 years  
older patients > 80 years in good overall condition

### **DBP < 90 mm Hg**

in all cases except diabetes (80 - 85 mm Hg)

Statistical analysis is boring, but it has valuable information ...

**Some statistical data**

# Why treat hypertension?

Prevalence in Czech republic 35%

Patients over 60 years > 50%

Reducing SBP by 10 mmHg and DBP by 5 mmHg

reduces stroke risk by 45%

reduces heart attack risk by 20%

reduces CV event risk by 33%

Metaanalysis of randomized clinical trials worldwide

# Treatment goals of hypertension

All population

BP below **140/90** mmHg

Diabetes

BP below **140/80-85** mmHg

Nephropathy with proteinuria  $\geq 1\text{g}$

SBP below **130** mmHg

# Target values during ambulatory BP monitoring

Ø 24 hours BP	< 130/80 mmHg
Ø BP during daytime	< 135/85 mmHg
Ø BP during sleep	< 120/70 mmHg
Systolic dipping	≥ 10 %

ABPM = 24 hours ambulatory blood pressure monitoring,  
dipping = BP drop in sleep

# Treatment goal of diabetes

**Primary prevention**

**HbA1c < 45 mmol/mol**

**Secondary prevention**

**HbA1c < 60 mmol/mol**

Secondary prevention + complicated (micro, macro) diabetes with high risk of hypoglycemia – increased CV risk in accurate compensation...according to clinical trials (ADVANCE, ACCOMPLISH), individual approach

HbA1c = glycosylated hemoglobin, standard = 20 – 37 mmol/mol, prediabetes = 38 – 47 mmol/mol, diabetes = over 48 mmol/mol (by SZÚ = NIPH = National Institute of Public Health)



# Treatment goal of hyperlipidemia

**Medium Risk**  
**(1-4 % SCORE)**

**LDL < 3,0 mmol/l**

**High Risk**  
**(5-9 % SCORE)**

**LDL < 2,5 mmol/l**  
**ApoB < 1,0 mmol/l**

**Very High Risk**  
**(≥ 10 % SCORE)**

**LDL < 1,8 mmol/l**  
**ApoB < 0,8 mmol/l**

Cholesterol binds to proteins apolipoproteins in the body and forms lipoproteins with them. LDL arises in the liver (size about 20 nm), contains apolipoprotein B responsible for cholesterol deposition.

# Current situation in Czech republic

60 -70 % hypertensive patients are treated

45 % pts treated achieve BP target values

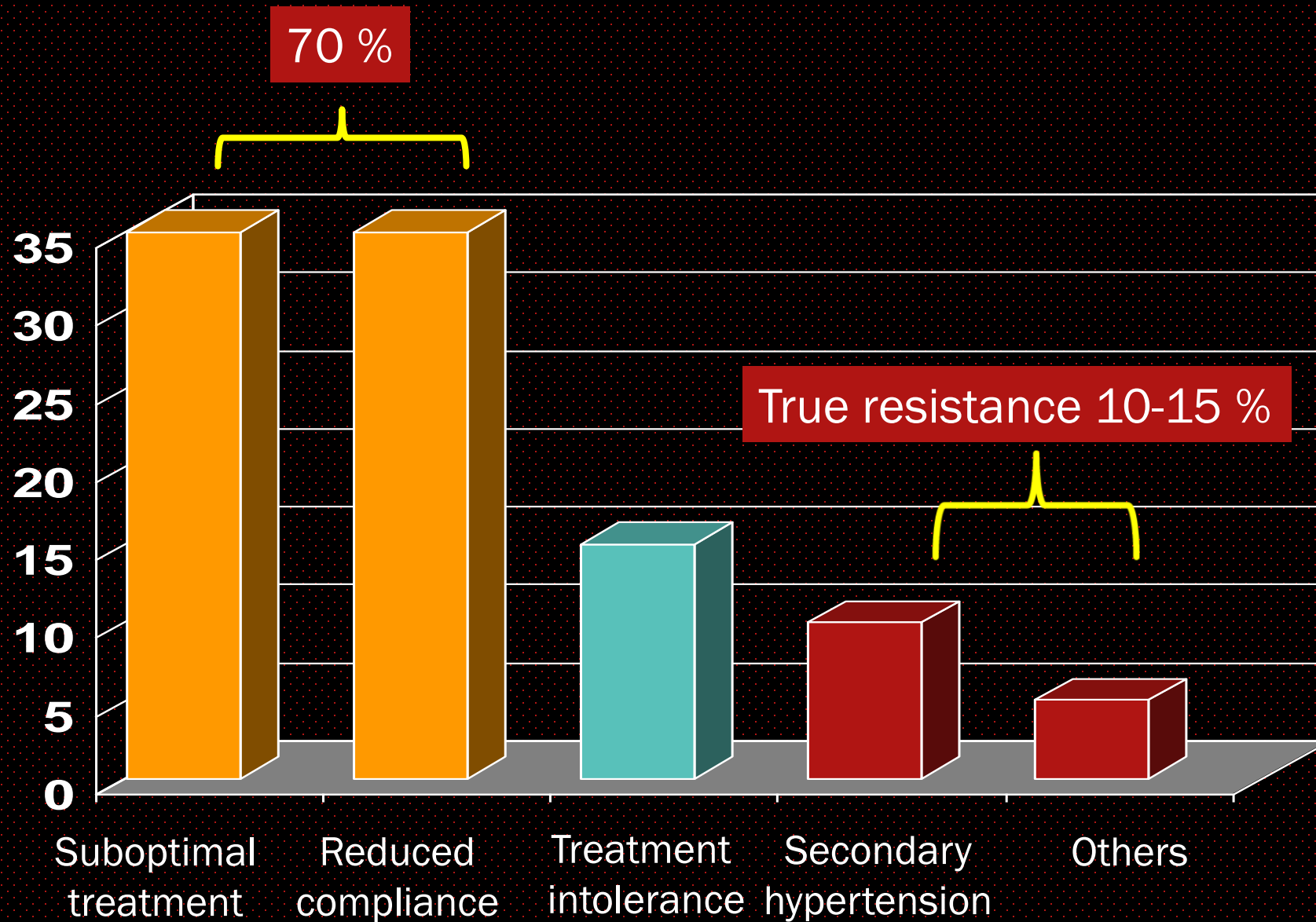
55 % pts treated don't achieve BP target values

# Current situation in Czech republic

What is the problem, that

55 % of treated patients don't achieve target BP?

# The most common causes of inadequate treatment



# The most common causes of secondary hypertension

- Renoparenchymal hypertension – after glomerulonephritis, nephropathy, polycystic kidney disease, chronic tubulointerstitial nephritis (analgetics, lithium) = positive laboratory findings in urine
- Primary hyperaldosteronism - aldosterone-producing adenoma (independent on axis RAAS)
- Pheochromocytoma - chromaffin cell tumor of the sympathetic NS, overproduction of catecholamines → arterial hypertension
- Cushing's syndrome – hypercortisolism → arterial hypertension
- Renovascular hypertension – more than 20% pts examined have renal artery stenosis
- Neurogenic hypertension – arises from vascular compression of the medulla oblongata, where are stored centers for blood pressure regulation.

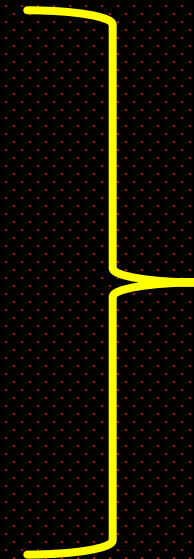
# The causes of poor control of hypertension and the high cardiovascular risk

Insufficient use of combinations

Insufficient use of fixed combinations

Complicated treatment schedule

Poor compliance



Physician

Patient

# Guidelines ESH/ESC 2013

Significantly Increased BP  
( $\geq 160/100$  mmHg)  
or high CV risk

**Treatment Initiation of 2 drugs combination**

BP  $\geq 140/90$  mmHg

Original combination of  
full dose

**Adding a third drug**

change to a different  
combination of the 2 drugs

**Combinations of  
3 drugs in  
full dose**

# How should be an ideal fixed combination ?

Combination of two or three drugs with long acting efficacy

Dosing of all components **once daily**

**Additive** antihypertensive effect, influencing other **pathogenic** mechanisms (AS, kidney, metabolism, increased heart rate, tissue effect)



# Most preferred combinations of the drugs

ACE-I or sartan

+

Dihydropyridine Ca blocker

+

Diuretic (not loop)

# Essential non-pharmacological treatment of arterial hypertension

1. Reduction

2. Limitation of

3. Decrease of

4. Increase of

5. Prohibition

6. Increased

Alcohol  
consumption

Smoking

Physical  
activity

Weight

Salt intake

Potassium  
intake

**And again the statistics...**

# Combination therapy of hypertension

To reach target blood pressure below 140/90 mmHg

→ combination is necessary in 70-80 % hypertensive pts

If the patient treated with adequate triple combination in adequate doses and taking prescribed medication

→ reaches the target BP below 140/90 mmHg in 90%.

**Case reports with interactive questions**

# Interactive questions

**2 questions** will be for each case study

The question is posed in the **title** of slide

There are **3 possible** answers, indicated by the numerals **1-3**

The correct answer is **only one**

I will show the correct answer on the next slide

# 1. Patient Z-M (M)

Man. Age 54 years, 180 cm, 96 kg, BMI: 29,6

**FH:** father heart attack in 60 years age    **PH:** Smoker: 10 cigarettes/day , chronic venous insufficiency grade III. **Hypertension:** since 1998, treated by combination **BB** (Lokren 20mg 1/2-0-0) + **ACEI** (Ramipril 5mg 1-0-0) + **Central drug** (Moxonidine 0,4 mg 1-0-1).

BP RUE seated: **158/98** Pulse: **62** reg, carotids without sound, CP comp., pulsation LE+

**Laboratory:** increased levels of lipids: CH **6,6** LDL **4,4** Tg **2,3**

Glycemia, K, UA and renal function in a standard. Urine + sed: no pathology.

**ECG** without signs of LV hypertrophy, normal

**ABPM:** hypertension daily with morning and late afternoon increase in blood pressure. Average of BP : **143/93 mmHg**

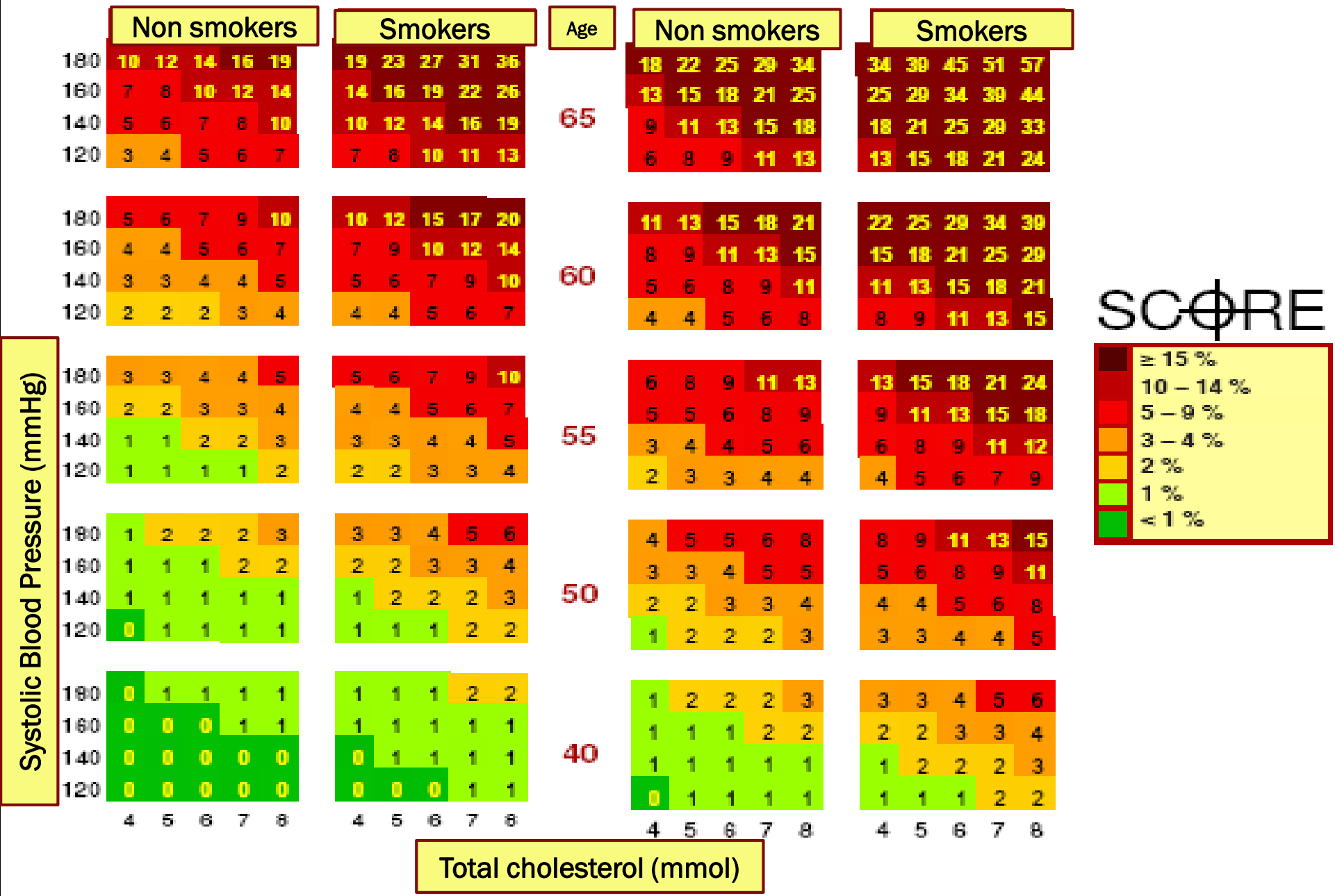
# Risk factors

- ▶ Age 54 years
- ▶ Gender Man
  
- ▶ SBP 158 mmHg
- ▶ Total cholesterol 6,6 mmol/l (LDL 4,4 mmol/l)
- ▶ Smoking Yes



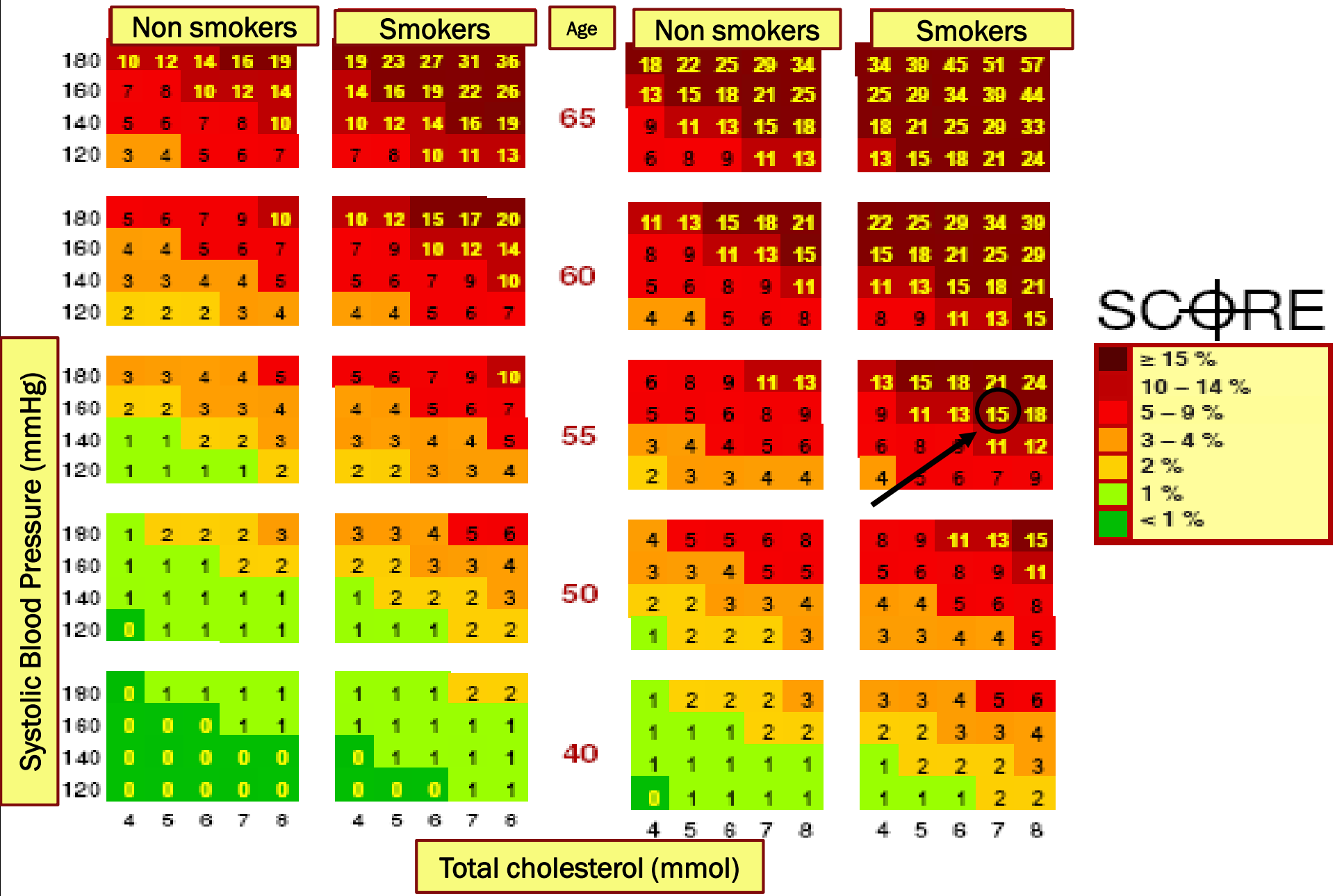
Women

Men



Women

Men



# 1. Patient Z-M (M)

**Dg:** I10 Hypertension with very high risk according to SCORE  
E782 Hyperlipoproteinemia mixed  
Overweight  
Chronic venous insufficiency grade III  
Smoking  
(risk SCORE **15** %, very high)

**Question 1. What is the target blood pressure, LDL and ABPM in this patient ?**

1. < 140/90 mmHg, < 3,0 mmol/l a < 130/85 mmHg
2. < 140/90 mmHg, < 2,5 mmol/l a < 130/90 mmHg
3. < 140/90 mmHg, < 1,8 mmol/l a < 130/80 mmHg

**Answer 1. What is the target blood pressure, LDL and ABPM in this patient ?**

1. < 140/90 mmHg, < 3,0 mmol/l a < 130/85 mmHg
2. < 140/90 mmHg, < 2,5 mmol/l a < 130/90 mmHg
3. < 140/90 mmHg, < 1,8 mmol/l a < 130/80 mmHg

**Question 2. What is the correct approach to adjusting the treatment of hypertension in this patient ?**

- 1. Add low dose diuretic into that combination**
- 2. Change medication on a fixed triple combination of ACEI, D, and CaB**
- 3. Change to a fixed combination of sartan and D and keep the BB and moxonidine**

**Answer 2. What is the correct approach to adjusting the treatment of hypertension in this patient ?**

- 1. Add low dose diuretic into that combination**
- 2. Change medication on a fixed triple combination of ACEI, D, and CaB**
- 3. Change to a fixed combination of sartan and D and keep the BB and moxonidine**

# 1. Patient Z-M (M)

**Goal:** BP above **140/90** mmHg, LDL < **1,8** ABPM above **130/80** mmHg

## **Treatment:**

**Non pharmacological:** weight reduction, diet - salt and fat limitation, endurance physical exercise, stop smoking

**Pharmacological:** (from 3 drugs to 1 tablet)

**ACE-I + D + Ca blocker** - Triplixam 10/2,5/5mg 1-0-0.

(Triplixam = perindopril arginin + indapamid + amlodipin)



# 1. Patient Z-M (M)

ACE-I + D + Ca blocker - Triplixam 10/2,5/5mg 1-0-0.

Why this treatment ?

ACE-I

- Antihypertensive and cardioprotective effect
- Vasoprotective and renal protective effect
- Positive effect on the carbohydrate metabolism
- Improve prognosis in HR patients with CHD, stroke, atherosclerosis and diabetes

Ca blockers

- Universal antihypertensive therapy
- Inducing systematic vasodilation
- no negative effects on lipid metabolism

Diuretics

- With long term effect, act in the distal tubule of the kidney, indapamide also has the strongest vasodilatory effect

(Triplixam = perindopril arginin + indapamid + amlodipin)

# 1. Patient Z-M (M)

Medical check up after 3 months:

Initial values : 158/98 mmHg, Pulse 62 reg, Weight 96 kg.

BP RUE seated: 136/86 mmHg Pulse: 70 reg, Weight: 94 kg, continues smoking

ABPM: curve adjustment in the morning and afternoon, the average BP 128/78 mmHg (orig.-143/93)

Lipids: cholesterol 6,4 LDL 3,6 (orig. - 4,4)

Dg: I10 High risk hypertension according SCORE

E782 Hypercholesterolemia mixed

Obesity, chronic venous insufficiency grade III

(risk SCORE 9 %, high risk)

Women

Men

Non smokers

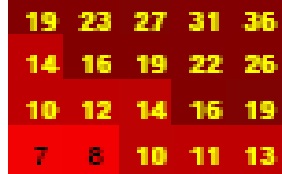
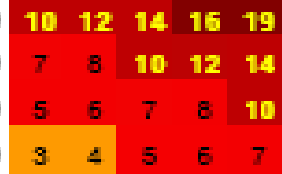
Smokers

Age

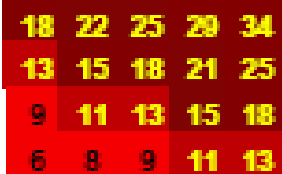
Non smokers

Smokers

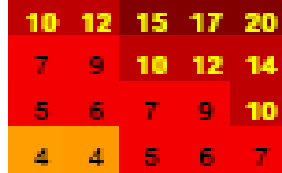
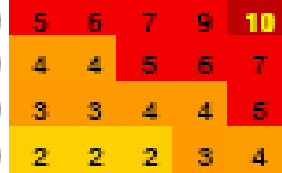
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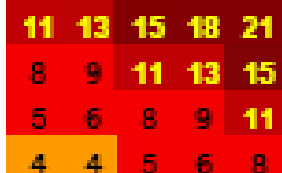
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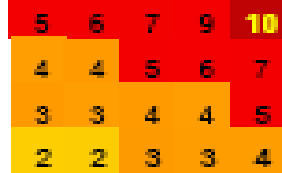
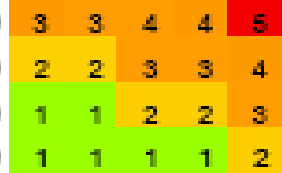
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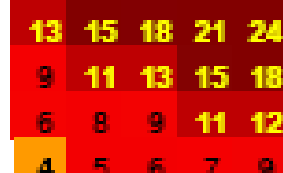
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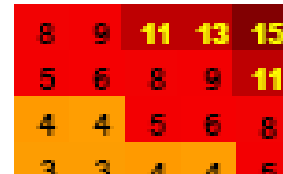
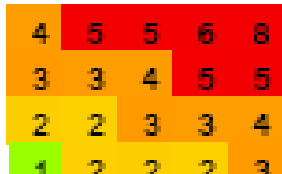
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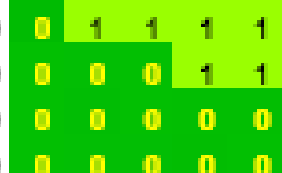
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Systolic Blood Pressure (mmHg)

4 5 6 7 8

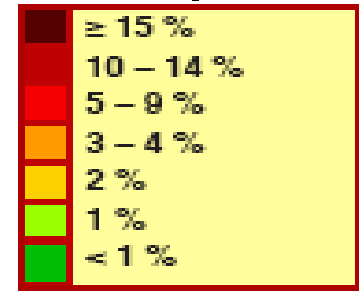
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Total cholesterol (mmol)

SCORE



Women

Men

Non smokers

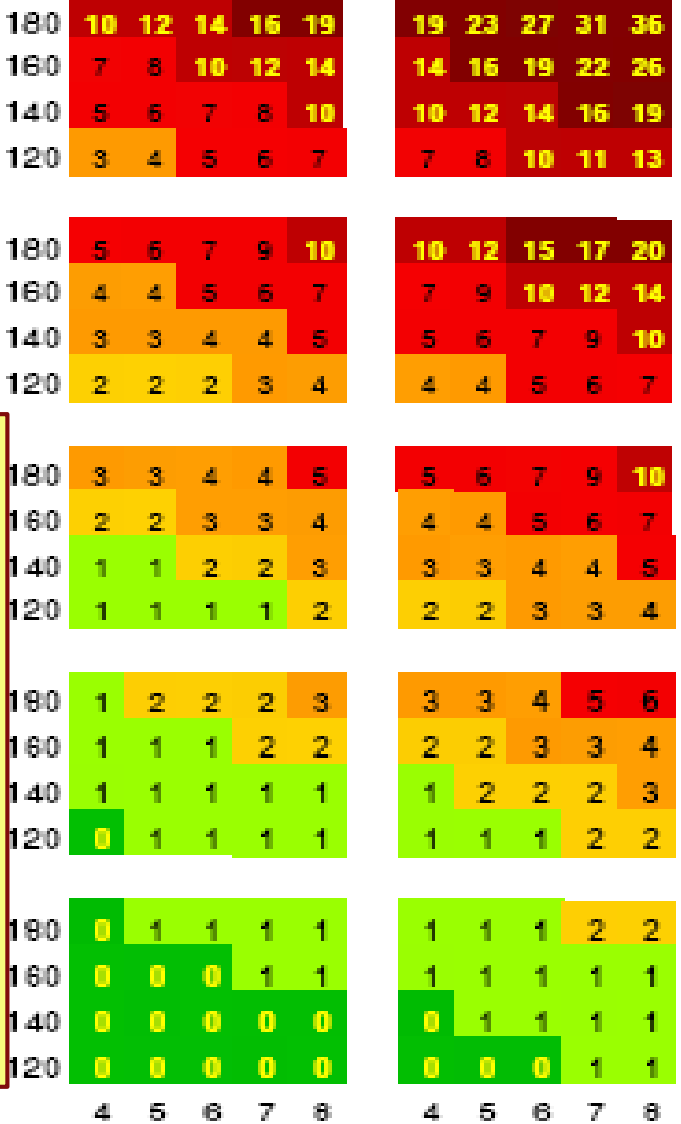
Smokers

Age

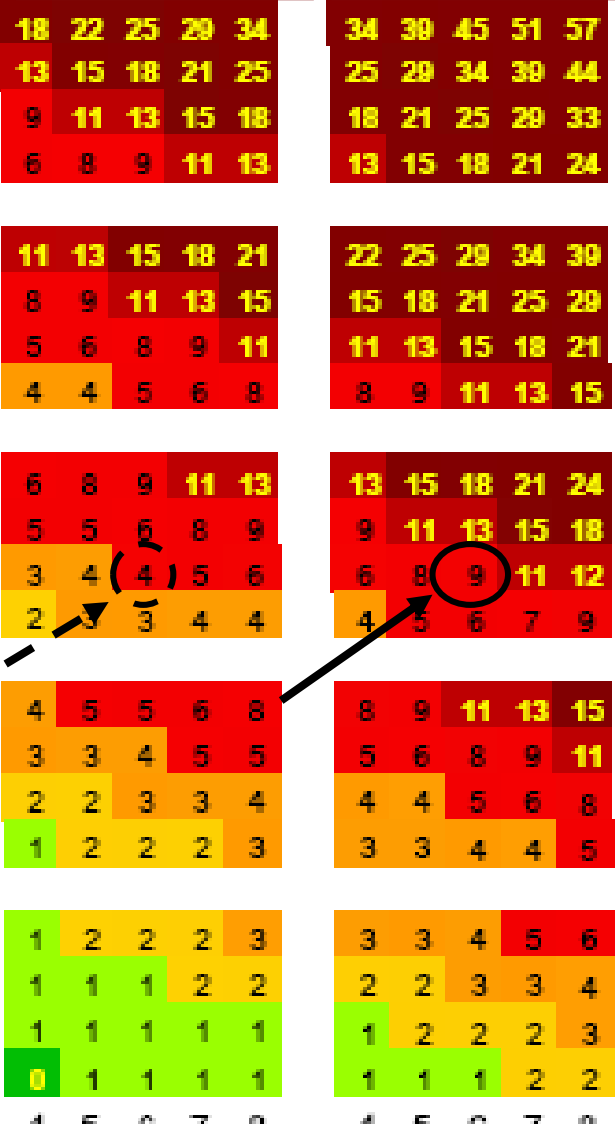
Non smokers

Smokers

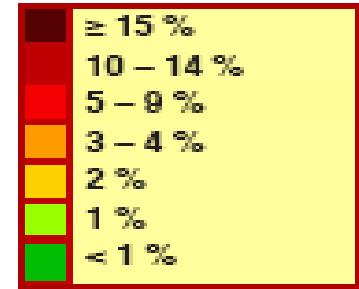
Systolic Blood Pressure (mmHg)



65  
60  
55  
50  
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SCORE



Total cholesterol (mmol)

# 1. Patient Z-M (M)

**Goal:** LDL < 2,5 mmol/l

## **Treatment:**

**Non pharmacological:** weight reduction, diet – salt and fat limitation, endurance physical exercise, stop smoking - continue to apply..

## **Pharmacological treatment:**

**Triplixam 10/2,5/5mg 1-0-0, Atorvastatin 20mg 1-0-0.**

## 2. Patient R-P (F)

Woman. Age **62** years old, 178 cm, **95** kg, BMI **30,6** FH: negative PH: 10 years **DM II** in PAD, 10 years **HLP** in statine therapy Abuse: non smoker **Hypertension** : since 10/1998 found during preventive inspection

**Clinical findings:** obesity with no any other pathology

BP seated: RUE **154/88** mmHg Pulse: **84** reg Waist: **108** cm

**Laboratory:** G **8,2** mmol/l HbA1c: **55** mmol/mol LDL **3,4** Urea, Creatinine, liver tests neg.

**ECG:** incomplete right bundle branch block

**ABPM:** daily hypertension, the average BP 24h: **142/78** mmHg, TF **80**.

**Microalbuminuria:** positive **45**mg/24h

**Treatment:** Concor 5mg 1-0-0, Agen 5mg 1-0-0, Lozap 50mg 1-0-1, Moduretic ½-0-0, Ebrantyl 60mg 1-0-1, Metformin 1000mg 1-0-1, Sortis 10mg 1-0-0.

# Risk factors

- ▶ Age 62 years old
- ▶ Gender Female
  
- ▶ SBP **154** mmHg
- ▶ Total cholesterol **5,9** mmol/l (LDL **3,4** mmol/l)
- ▶ Smoking No
  
- ▶ Diabetes with positive albuminuria (**multiplies risk 3 - 5 times**)

Women

Men

Non smokers

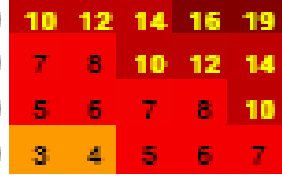
Smokers

Age

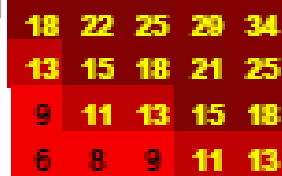
Non Smokers

Smokers

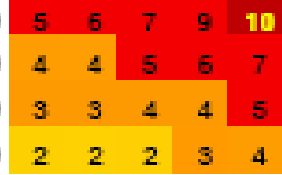
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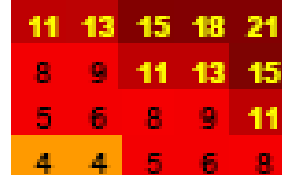
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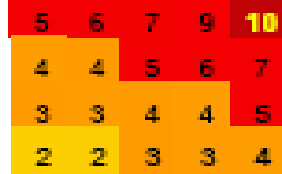
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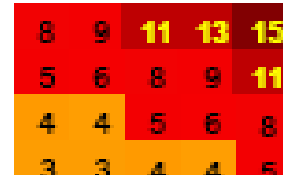
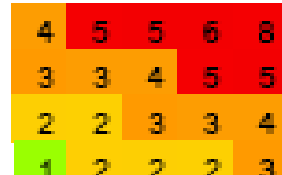
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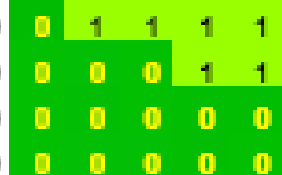
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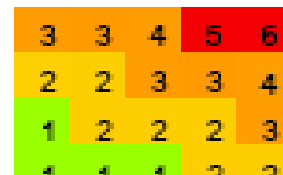
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Systolic Blood Pressure (mmHg)

4 5 6 7 8

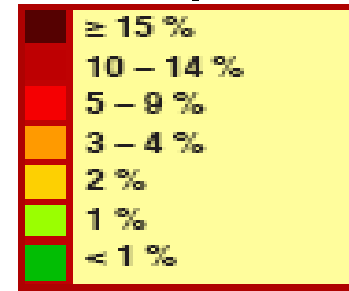
4 5 6 7 8

4 5 6 7 8

4 5 6 7 8

Total cholesterol (mmol)

SCORE





Women

Men

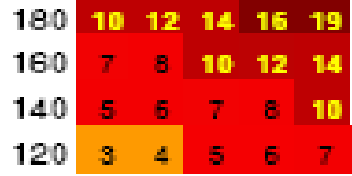
Non smokers

Smokers

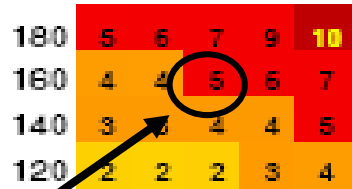
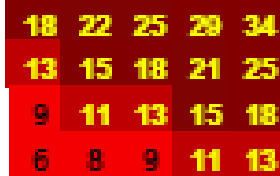
Age

Non Smokers

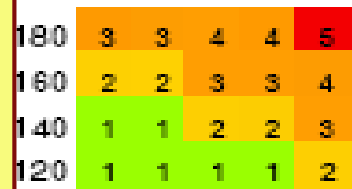
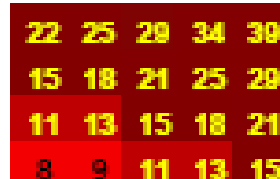
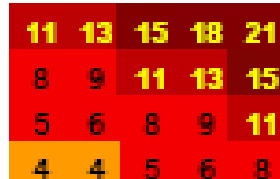
Smokers



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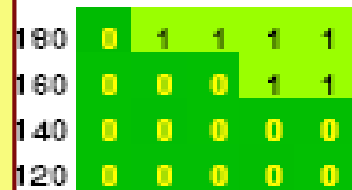
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Systolic Blood Pressure (mmHg)

4 5 6 7 8

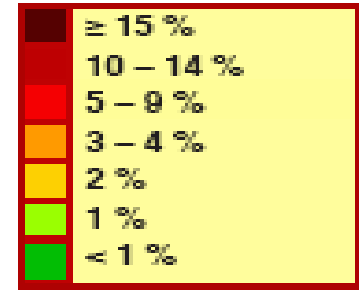
4 5 6 7 8

4 5 6 7 8

4 5 6 7 8

Total cholesterol (mmol)

SCORE



## 2. Patient R-P (F)

Dg: I10 Hypertension with high risk according to SCORE more systolic

E112 DM II type in PAD with renal complications (albuminuria)

E782 Mixed hyperlipoproteinemia

Obesitas, Metabolic syndrome

**Risk SCORE 5 % (3 to 5 times higher, DM II and albuminuria, very high)**

**Question 1. What is the target blood pressure, LDL and HBA1c in this patient ?**

**1. BP < 140/80-85 LDL < 1,8 a HBA1c < 45**

**2. BP < 140/90 LDL < 2,5 a HBA1c < 45**

**3. BP < 130/80 LDL < 2,5 a HBA1c < 60**

## Answer 1.

What is the target blood pressure, LDL and HBA1c in this patient ?

**1. BP < 140/80-85 LDL < 1,8 a HBA1c < 45**

**2. BP < 140/90 LDL < 2,5 a HBA1c < 45**

**3. BP < 130/80 LDL < 2,5 a HBA1c < 60**

**Question 2. What is the drug of first, second and third choice for AH in this patient ?**

- 1. ACE-I/sartan + Ca/B + indapamid**
- 2. CaB + ACEI/sartan + indapamid**
- 3. ACEI/sartan + indapamid + BB**

**Answer 2. What is the drug of first, second and third choice for AH in this patient ?**

- 1. ACE-I/sartan + CaB + indapamid**
2. CaB + ACEI/sartan + indapamid
3. ACEI/sartan + indapamid + BB

## 2. Patient R-P (F)

ACE-I + D + Ca blocker - Triplixam 10/2,5/5mg 1-0-0.

Why this treatment?

**ACE Inhibitors and AT1-receptor blockers** in diabetic patients with AH can:

- delay terminal renal failure
- slow down the progression of microalbuminuria / proteinuria
- best combination of two antihypertensives ACE inhibitor is considered to be (and probably also the AT1-receptor blocker) with a Calcium channel blocker

**Diuretic induces** volume depletion and reduce the sodium concentration, which leads to activation of the RAA system. ACEi act synergistically and can thus significantly reduce hypertension,

**Ca blockers** induce systemic vasodilation, **no negative effects on lipid metabolism**

**Beta blocker** is allowed to decrease heart rate

Triplixam = perindopril arginin, indapamid, amlodipin, Eucreas = metformin + vidagliptin

## 2. Patient R-P (F)

**Goal:** weight reduction BMI under 25, BP under 140/80-85 mmHg, LDL under 1,8 mmol/l, HBA1c under 45 mmol/mol.

### **Treatment:**

Non pharmacological: weight reduction, endurance physical exercise, salt, sugar and fats limitation in diet

Pharmacological: (reduction from 9,5 to 5 pills)

Triplixam 10/2,5/10mg 1-0-0, Concor 5mg 1-0-0, Eucreas 50/1000mg 1-0-1, Sortis 40mg 1-0-0.

Triplixam = perindopril arginin, indapamid, amlodipin, Eucreas = metformin + vidagliptin



## 2. Patient R-P (F)

Medical check-up after 3 months:

Initial values: BP 154/88, Pulse 84 reg, Weight 95 kg, LDL 3,4 gly 8,2, HbA1c 55%

BP RUE seated: 136/76 mmHg Pulse 80 reg Weight: 95 kg Waist 100 cm

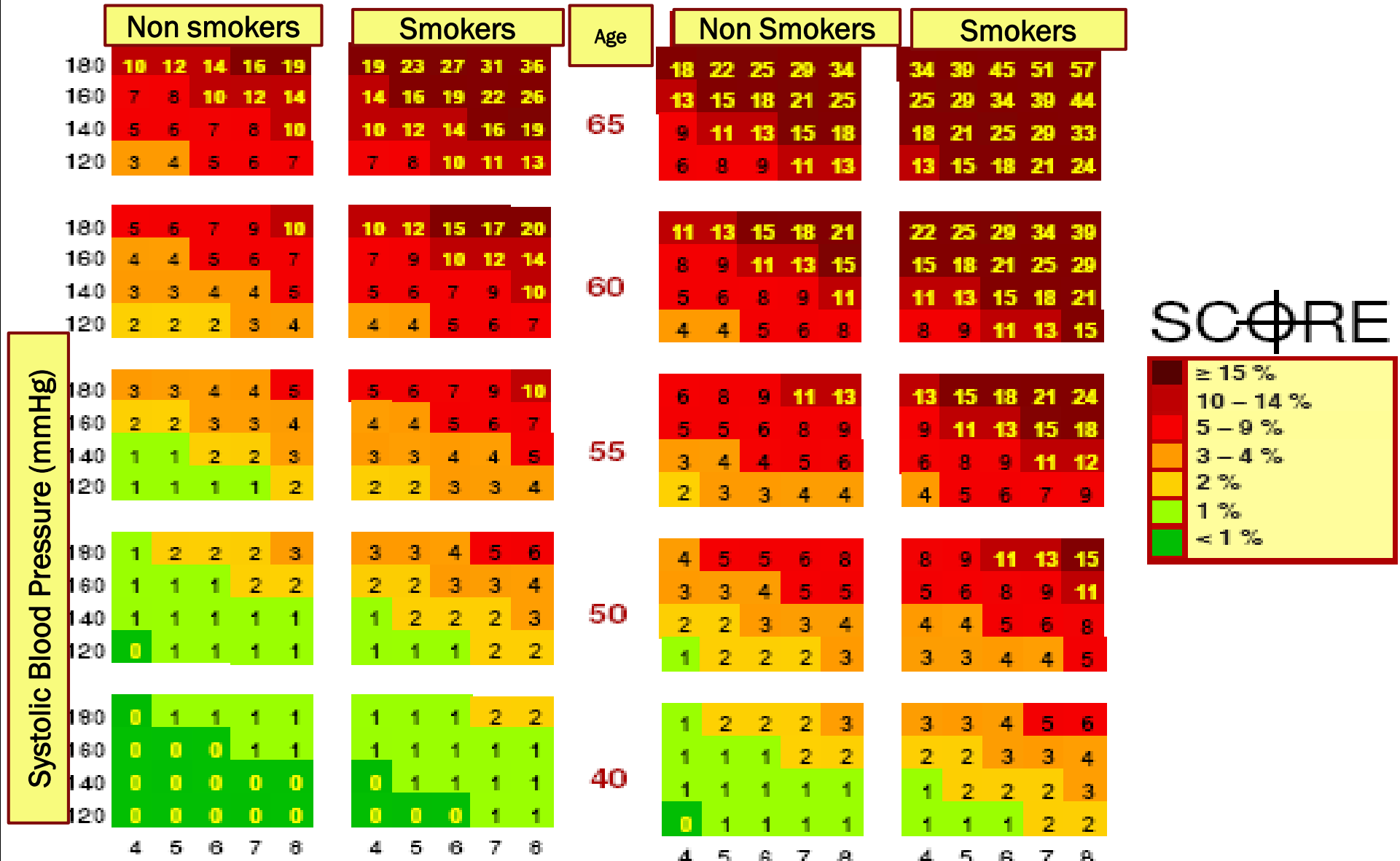
Lipids: LDL 1,9 Glycemia: 5,8 mmol/l HbA1c 48 %

**Treatment:** Treatment unchanged, kept well

Triplixam 10/2,5/10mg 1-0-0, Concor 5mg 1-0-0, Eucreas 50/1000mg 1-0-1,  
Sortis 40mg 1-0-0.

Women

Men

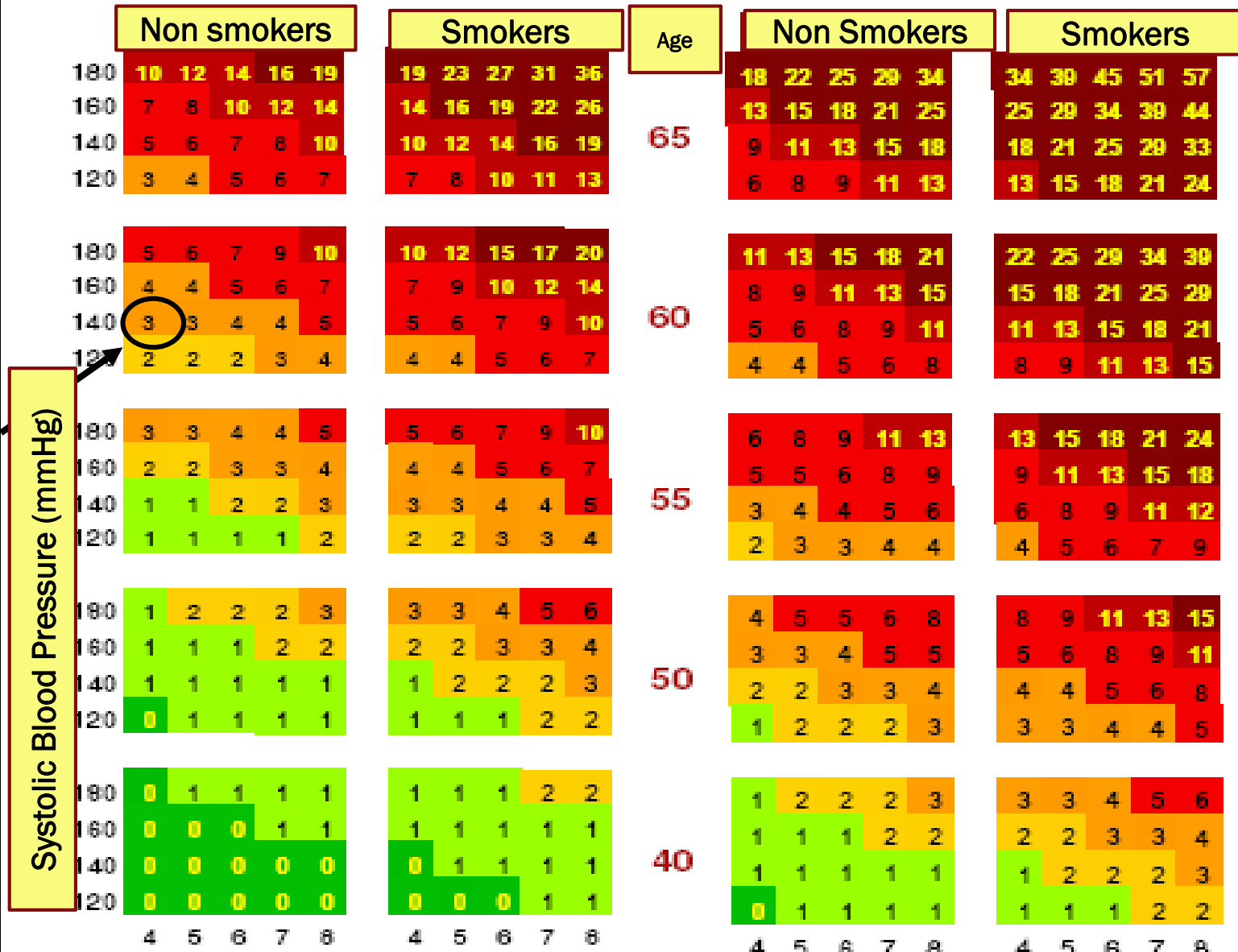


Systolic Blood Pressure (mmHg)

Total cholesterol (mmol)

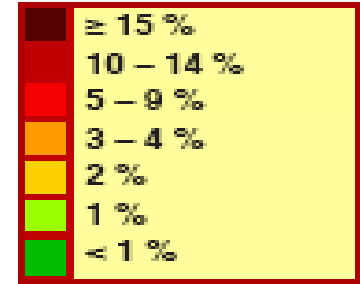
Women

Men



DM II type  
High Risk !!

SCORE



Total cholesterol (mmol)

### 3. Patient J-K (M)

Man. Age 44 years, 172 cm 72 kg, BMI: 24,3

**FH:** father heart attack in 45 years **PH:** Non smoker, hypertensive nephropathy 5 years, proteinuria 1,1 g/24h, **Hypertension:** since 1990, treated by combination ACEI/CaB (Prestance 5/5mg 1-0-0) + D (Moduretic 50/5 mg 1/2-0-0) + BB (Concor 10mg 1-0-0).

BP RUE seated: 138/86 Pulse 64 reg, carotids without sound, cardiopulm. comp., pulse in LE+

**Laboratory:** lipids CH 4,8 LDL 2,9 Tg 1,6

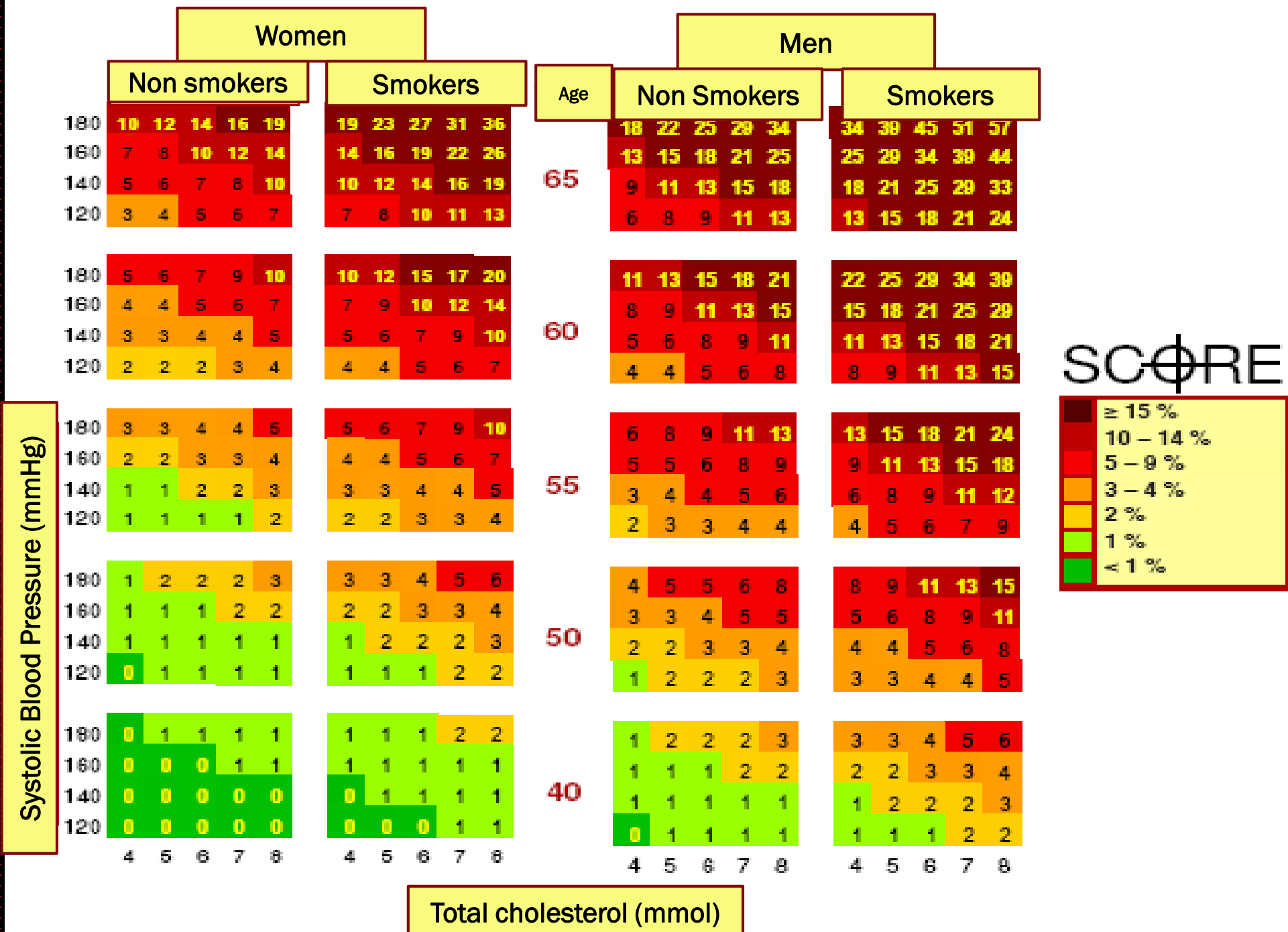
Glycemia, K, normal. Krea: 110 umol/l GFR 54ml/min/m<sup>2</sup> urine and sediment: proteinuria, no other pathology.

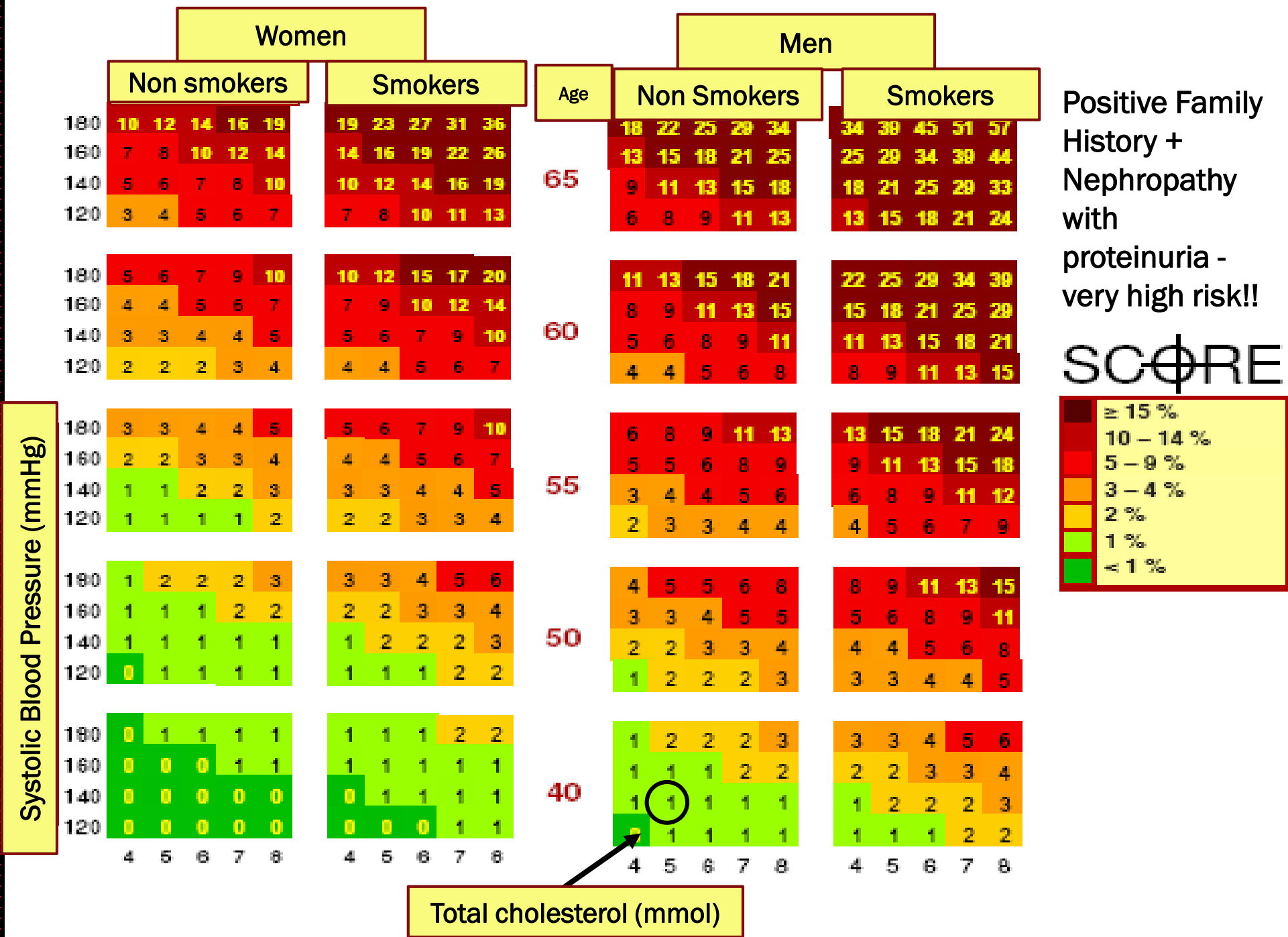
**ECG:** no signs of LV hypertrophy, finding normal

**ABPM:** normotension, without night decline of BP, Average 24h 128/77, day 129/78, night 127/76 mmHg

# Risk factors

- ▶ Age 44 years
- ▶ Gender Man
  
- ▶ SBP **138** mmHg
- ▶ Total cholesterol **4,8** mmol/l (LDL **2,9** mmol/l)
- ▶ Smoking No
  
- ▶ Nephropathy with proteinuria more than 1g – **very high risk, secondary prevention**





### 3. Patient J-K (M)

**Dg:** I10 Hypertension with very high risk according to SCORE,  
non-dipping

N189 Nephropathy (hypertensive ?), CKD G3a, A3 (next slide)

(risk SCORE 1-2 %, nephropathy with proteinuria, very high !!!, ↑ night BP)



# CKD - Chronic kidney disease classification

Stage	Description	GFR (ml/min/1,73 m <sup>2</sup> )	Clearance ml/s
G1	Normal KF	up to 90	up to 1,5
G2	Mildly reduced KF	60 – 89	1,0 – 1,5
G3a	Moderately reduced KF	40 – 59	0,75 – 0,99
G3b	Moderately reduced KF	30 – 39	0,5 – 0,74
G4	Severely reduced KF	15 – 29	0,26 – 0,49
G5	Very severe, endstage kidney failure	under 15	under 0,25

Time duration longer than 3 months under 60 ml/min (formula CKD-EPI), correction by CNS – Czech Nephrology Society 2014, <http://www.nefrol.cz/odbornici/doporucene-postupy-cns>

# GF, albuminuria a CV risk

<b>CKD prognosis: According to GF categories(ml/min) and albuminuria (mg/mmol krea) or (mg/24 hours)  KDIGO 2012</b>		<b>Albuminuria categories</b>		
		A1 (standard under 1,5 mg/mmol)	A2 (albuminuria)	A3 (proteinuria)
		Standard or slightly increased	Moderately increased	Severely increased
		< 3 mg/mmol < 30mg/24 h	3 – 30 mg/mmol 30 – 300 mg/24h	> 30 mg/mmol > 300 mg/24h
G1	up to 90	Low risk	Medium risk	High risk
G2	60 – 89			
G3a	40 – 59			Very high risk
G3b	30 – 39			
G4	15 – 29			
G5	under 15			

Calculation must take into account the associated diseases

Correction according to <http://www.nefrol.cz/odbornici/doporucene-postupy-cns> 2014

## Question 1.

**What is the target value of BP, LDL and night ABPM?**

1. < 140 mmHg, < 3,0 mmol/l a < 130/80 mmHg
2. < 130 mmHg, < 1,8 mmol/l a < 120/70 mmHg
3. < 140 mmHg, < 2,5 mmol/l a < 125/75 mmHg

Answer 1.

What is the target value of BP, LDL and night ABPM?

1. < 140 mmHg, < 3,0 mmol/l a < 130/80 mmHg
2. < 130 mmHg, < 1,8 mmol/l a < 120/70 mmHg
3. < 140 mmHg, < 2,5 mmol/l a < 125/75 mmHg

## Question 2.

What is the correct approach to adjusting the treatment of AH in this patient ?

1. To add alpha 1 blocker to this combination
2. Fixed triple combination ACEI, D and CaB + BB, additional CaB in the evening
3. Replace Moduretic for a loop diuretic + verospiron

## Question 2.

What is the correct approach to adjusting the treatment of AH in this patient ?

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3. Replace Moduretic for a loop diuretic + verospiron

### 3. Patient J-K (M)

**Goal:** SBP under **130** mmHg, LDL < **1,8** ABPM night under **120/70** mmHg

#### **Treatment:**

**Non pharmacological:** salt and fat limitation, endurance physical exercise.

**Pharmacological:** evening dose of AH therapy is required, from 2,5 pills to 4 pills

**Triplixam 10/2,5/5mg 1-0-0, Concor 10mg 1-0-0, Zorem 5mg 0-0-1, Sortis 20mg 1-0-0.**

(Triplixam = perindopril arginin + indapamid + amlodipin)

### 3. Patient J-K (M)

Medical check-up after 3 months:

BP RUE seated: **126/84** mmHg Pulse **60** reg

**ABPM:** improving BP curve in the night, 24h BP 122/76, day 124/78, night **118/71** mmHg (remain non – dipper)

**Lipids:** LDL **1,7** Creatinine: 106 umol/l, **GFR 58 ml/min/m<sup>2</sup>**

**Dg:** I10 Hypertension with very high risk according ESH 2013, dipping improved  
N189 Nephropathy with retention of nitrogenous substances, proteinuria, CKD  
G3a, A3 GF 58 ml/min



# Conclusions

Achieving target BP values is current priority of antihypertensive treatment

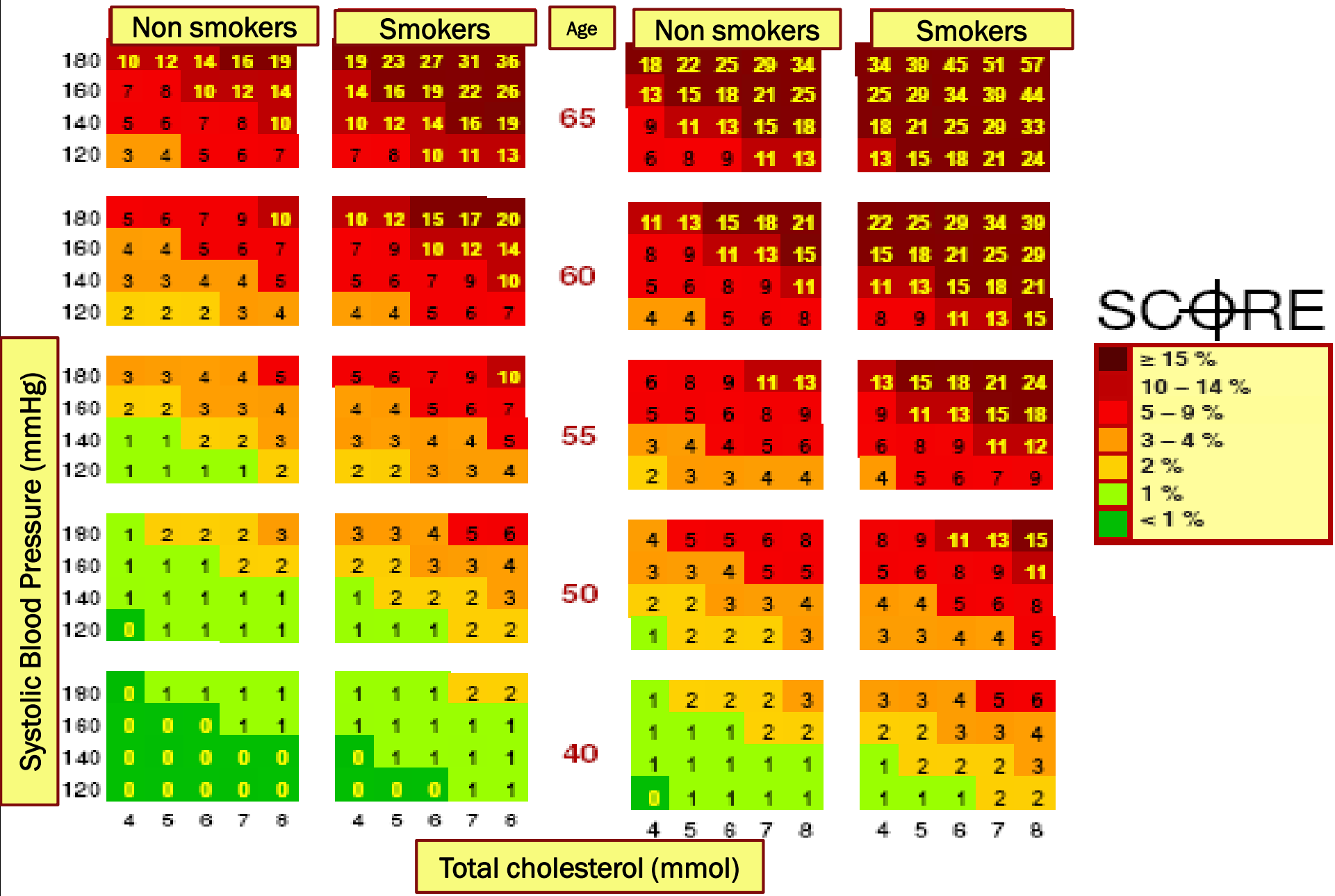
The most common causes of inadequate control of blood pressure is inadequate treatment and poor adherence.

The majority of patients (70-80%), need combination therapy to achieve normalization of blood pressure.

Fixed combinations reduce the number of tablets and improve access to treatment (EBM recommendations).

Women

Men



# Physiological Parameters

<b>Glycaemia:</b>	3,33 - 5,59 mmol/l,
<b>Total cholesterol:</b>	2,90 - 5,00 mmol/l
<b>TG:</b>	0,45 - 1,70 mmol/l – atherogenic lipids
<b>HDL:</b>	1,20 - 2,70 mmol/l -
<b>LDL:</b>	1,20 - 3,00 mmol/l – atherogenic lipids

**Waist:** – better indicator than BMI.

Men : risky up to 94 cm, very high risk up to 102 cm

Women: maximum 80 cm, very high risk up to 88 cm.