



# Hormon tedavisi ile kardiyoproteksiyon sağlayabiliyor muyuz?

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Bu sunumda herhangi bir firma/şahıs destek ilişkisi bulunmamaktadır

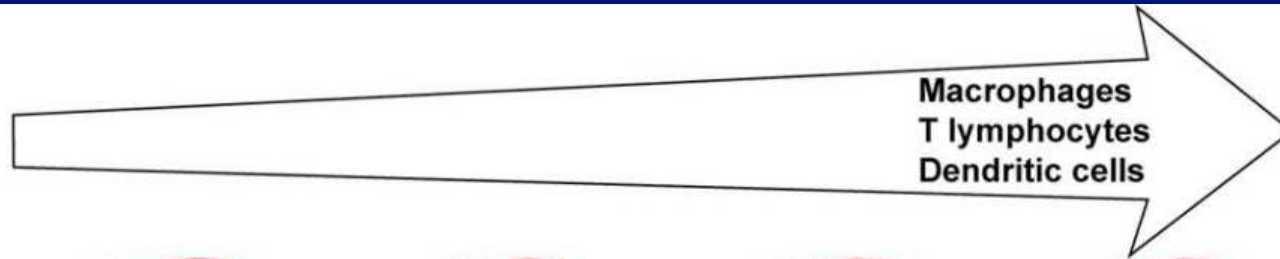
# Kardiyovasküler Hastalıklar (KVH)

- 50 yaşın üzerindeki kadın mortalitesinin %40'ından sorumlu

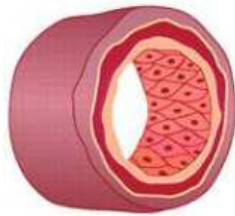
(meme Ca ise %5'inden!)

# Aterosklerozis

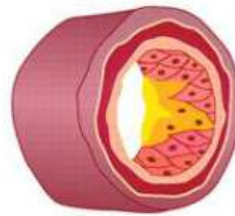
- **Progresif süreç**
- **Temel 4 evresi var**
  - Evre 1: Endotel hasarı ör. TA↑, LDL, Lp(a)
  - Evre 2: Plak oluşum başlangıcı (köpük hücreleri)
  - Evre 3: İnflamasyon (IL6, TNFa, CRP, PAI, E-selektin, ICAM-1)
  - Evre 4: Plak rüptürü ve Tromboz (MMP-9)



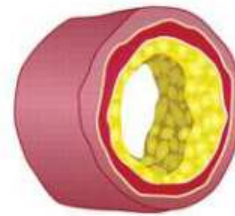
**Pathology**



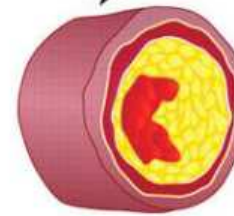
Healthy artery



Fatty streak



Atherosclerotic plaque



Plaque rupture or erosion + thrombus formation

**Clinical stage**

Asymptomatic

Asymptomatic

Asymptomatic or angina (CCS I-IV)

ACS

1° prevention

2° prevention

**Anti-inflammatory therapies:**

Current:

Statins

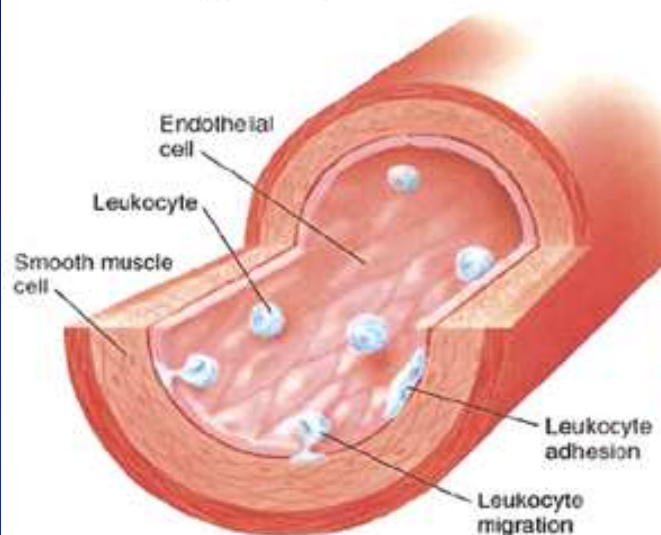
Statins

Experimental:

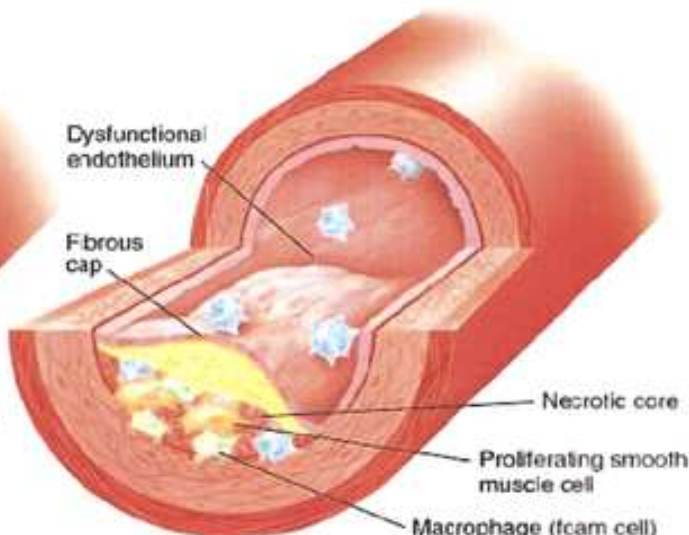
Immunization

- Antagonists of TNF superfamily
- IL-1Ra antagonists
- IL-6R antagonists
- Very low dose methotrexate (VLDM)
- Fingolimod (FTY720)
- Leukotriene antagonists
- Chemokine antagonists/heteromers
- Regulatory T cell expansion
- Immunization

### Early atherogenesis



### Established atherosclerosis



#### Beneficial effects of HRT

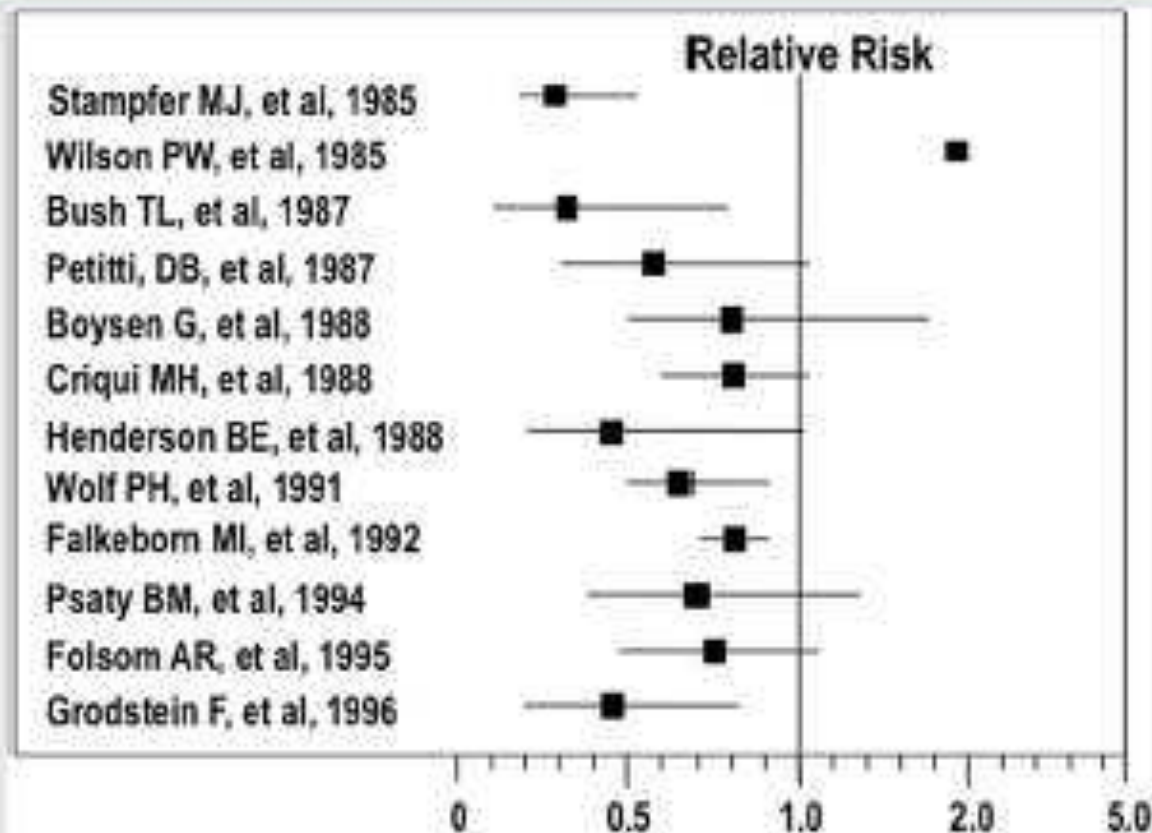
- ↑ Vasodilation
- ↑ Nitric oxide
- ↓ Endothelin
- ↑ Cox-2
- ↓ Inflammatory activation
- ↑ Nitric oxide
- ↓ CAMs
- ↓ MCP-1, TNF- $\alpha$
- ↓ Lesion progression
- ↑ Nitric oxide
- ↓ Inflammatory cell adhesion
- ↓ LDL oxidation/binding
- ↓ Platelet activation
- ↓ VSMC proliferation

#### Altered biology of HRT

- ↓ ER expression, function
- ↓ Vasodilation
- ↑ Inflammatory activation
- ↑ Plaque instability
- ↑ MMP
- ↑ Neovascularization

# Kohort ve Gözlemsel çalışmalarda KVH olay riskleri

**FIGURE 1**



- MHT verilmesi ile 11 gözlemsel çalışmada azalmış KVH olayı riski
- Bunların 5'inde istatistiksel olarak belirgin risk azalması (%40-50!)

# MHT -Gözlemsel çalışmalar

1. Endojen östrojenleri azalmış kadınların, fonksiyonel overleri olanlara göre KVH riski FAZLA
2. MHT, posmenopozal kadınlarda KVH görülme sıklığını azaltıyor

# Randomize Klinik Çalışmalar

- 1995..PEPI (Postmenopausal Estrogen/ Progestin Intervention)... primer
- 1998..HERS (Heart and Estrogen/ Progestin Replacement Study)... sekonder
- 2002..WHI (Women's Health Initiative)... primer

	RCT	Observasyonel Çalışmalar
Çalışma başlangıcındaki yaş (yıl)	>62	30-55
Menopoz süresi (yıl)	>10	<6
Tedavi süresi (yıl)	<7	>10
Menopozal semptomlar (ateş basması)	hariç	mevcut
Vücut Kitle İndeksi (ort, kg/m <sup>2</sup> )	29	25

# WHI

Outcomes—relative risk (RR) of outcome in treatment arm

	WHI-E + P trial		WHI-E trial	
	Age group (years)	RR (95% CI)	Age group (years)	RR (95% CI)
Coronary heart disease	50–59	1.34 (0.82–2.19)	50–59	0.60 (0.35–1.01)
	60–69	1.01 (0.73–1.39)	60–69	0.95 (0.72–1.24)
	70–79	1.31 (0.93–1.84)	70–79	1.09 (0.8–1.49)
Myocardial infarction	50–59	1.32 (0.77–2.25)	50–59	0.55 (0.31–1.0)
	60–69	1.05 (0.74–1.47)	60–69	0.95 (0.69–1.3)
	70–79	1.46 (1.00–2.15)	70–79	1.24 (0.88–1.75)
Stroke	50–59	1.51 (0.81–2.82)	50–59	0.99 (0.53–1.85)
	60–69	1.45 (1.00–2.11)	60–69	1.55 (1.10–2.16)
	70–79	1.22 (0.84–1.79)	70–79	1.29 (0.9–1.86)

# Yeni RKÇlar

- Danish Osteoporosis Study (DOPS) (2012)...MI, kalp yetmezliği
- Kronos Early Estrogen Prevention Trial (KEEPS) (2014)... Subklinik ateroskleroz progresyonu
- Early versus Late Intervention Trial with Estrogen (ELITE) (...)...Erken ateroskleroz progresyonu

1. Menopozal hormon tedavisi (MHT) ile primer kardiyak koruma sağlanabilir mi?

Uygun olgularda yararlı

2. Menopozal hormon tedavisi (MHT) ile sekonder kardiyak koruma sağlanabilir mi?

HAYIR

3. Menopozal hormon tedavisi (MHT) kardiyak olumlu etki için hangi faktörler önemli?

Semptomatik ve KVH açısından düşük riskli, menopozdan sonraki ilk 10 yıldaki 60 yaşından küçük olgular

Significant symptoms of menopause (moderate-to-severe hot flashes, night sweats)?<sup>b</sup>

No

Avoid HT

Yes

Free of contraindications<sup>c</sup> to HT and no h/o CHD, stroke, or TIA?  
AND  
No increased risk of stroke (<10% by Framingham Stroke Score)?<sup>d</sup>

Yes

No

Assess CHD risk and years since last menstrual period

Avoid HT<sup>e</sup>

CHD Risk Over 10 Years  
(Framingham CHD Risk Score)<sup>e</sup>

	Years Since Last Menstrual Period <sup>f</sup>		
	≤5	6 to 10	>10
Very low (<5%)	HTOK	HTOK	Avoid HT
Low (5% to <10%)	HTOK	HTOK (Choose transdermal) <sup>g</sup>	Avoid HT
Moderate (10% to 20%)	HTOK (Choose transdermal)	HTOK (Choose transdermal) <sup>g</sup>	Avoid HT
High (more than 20%)	Avoid HT	Avoid HT	Avoid HT

DECISION ABOUT DURATION OF USE: continued moderate-to-severe symptoms; patient preference; weigh baseline risks of breast cancer vs osteoporosis

# Sonuç

- Kalp krizi riskini azaltmak için MHT verilmesi önerilmez
- $\geq 60$  yaş veya menopoz süresi  $\geq 10$  yıl olan olgularda MHT başlanması önerilmez
- Kalp hastalığı varsa veya riski mevcut ise MHT önerilmez

29 Ekim

CUMHURİYET  
BAYRAMI

BU SEVGİ HİÇ BİTMEYEBEK

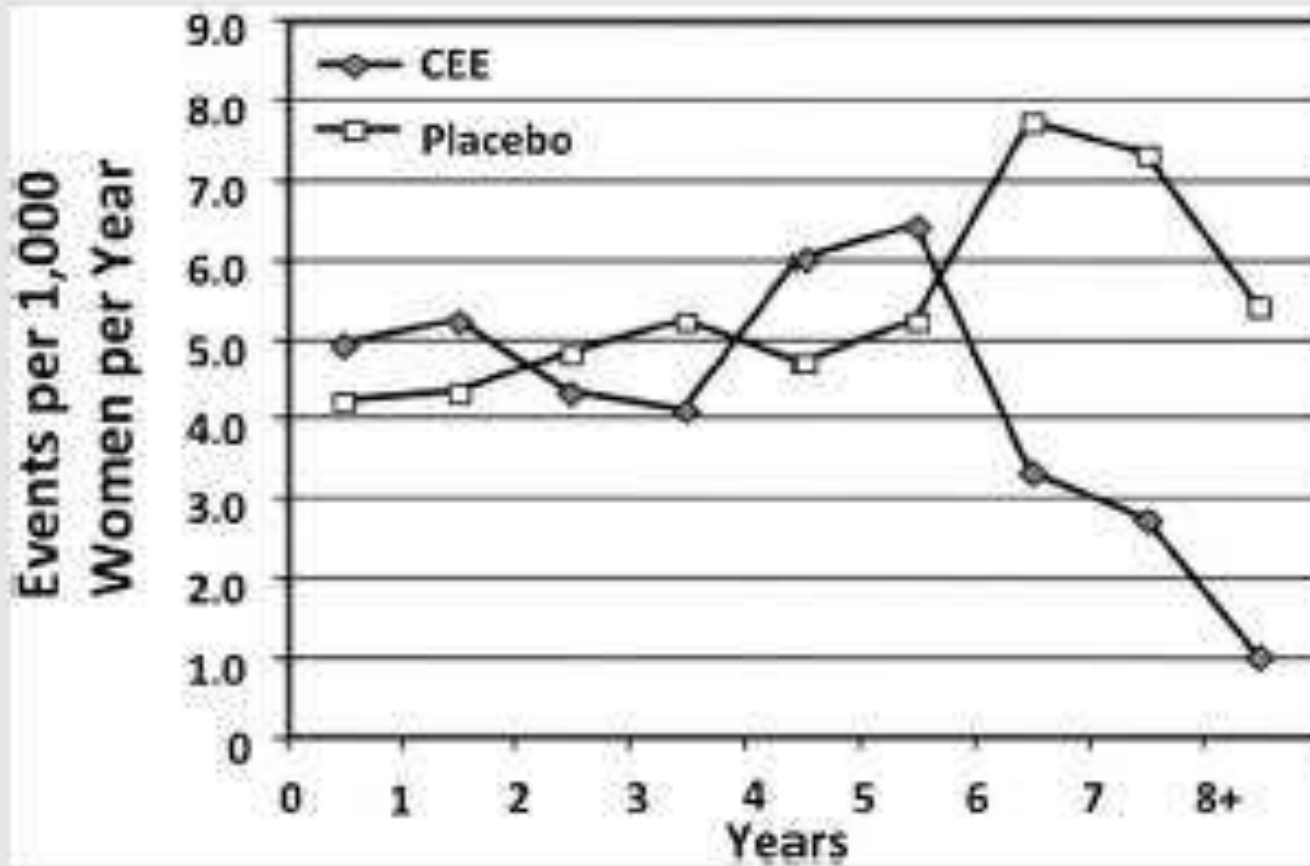


*Teşekkürler...*



- [www.HeartScore.org](http://www.HeartScore.org)
- <http://cvdrisk.nhlbi.nih.gov/>

**FIGURE 2**





# FRAMINGHAM RISK SCORE to predict 10 year ABSOLUTE RISK of CHD EVENT

ST ALBANS & HEMEL HEMPSTEAD NHS TRUST : CARDIOLOGY DEPARTMENT



This risk assessment only applies to assessment for PRIMARY PREVENTION of CHD, in people who do not have evidence of established vascular disease. Patients who *already* have evidence of vascular disease usually have a >20% risk of further events of over 10 years, and require vigorous SECONDARY PREVENTION. People with a Family History of premature vascular disease are at higher risk than predicted; Southern Europeans and some Asians may have a lower risk in relation to standard risk factors.

**STEP 1: Add scores by sex for Age, Total Cholesterol, HDL-Cholesterol, BP, Diabetes and Smoking.** (If HDL unknown, assume 1.1 in Males, 1.4 in Females)

Age			Total Cholesterol			HDL Cholesterol			Systolic BP		Diastolic BP					Diabetes			Smoking		
	M	F		M	F		M	F	Male	<80	80-84	85-89	90-99	≥100	No	M	F	No	M	F	
30-34	-1	-9	< 4.1	-3	-2	< 0.9	2	5	<120	0	0	1	2	3	No	0	0	No	0	0	
35-39	0	-4	4.1 - 5.1	0	0	0.9 - 1.16	1	2	120-129	0	0	1	2	3	Yes	2	4	Yes	2	2	
40-44	1	0	5.2 - 6.2	1	1	1.17 - 1.29	0	1	130-139	1	1	1	2	3							
45-49	2	3	6.3 - 7.1	2	1	1.30 - 1.55	0	0	140-159	2	2	2	2	3							
50-54	3	6	7.2	5	3	≥1.56	-2	-3	≥160	3	3	3	3	3							
55-59	4	7							Female	<80	80-84	85-89	90-99	≥100							
60-64	5	8							<120	-3	0	0	2	3							
65-69	6	8							120-129	0	0	0	2	3							
70-74	7	8							130-139	0	0	0	2	3							
									140-159	2	2	2	2	3							
									≥160	3	3	3	3	3							

If Systolic and Diastolic BP fall into different categories, use score from higher category

Categorisation of 10 year Risk of CHD Event	
Very Low risk	< 10%
Low risk	< 15%
Moderate risk	15-20%
High risk	> 20%

**STEP 2: Use total score to determine Predicted 10 year Absolute Risk of CHD Event (Coronary Death, Myocardial infarction, Angina) by sex**

Total Score	≤-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	≥17
10 year Risk: Male		<2%	3%	3%	4%	5%	7%	8%	10%	13%	16%	20%	25%	31%	37%	45%	53%	53%	53%	53%
10 year Risk: Female	<1%	2%	2%	2%	3%	3%	4%	4%	5%	6%	7%	8%	10%	11%	13%	15%	18%	20%	24%	27%

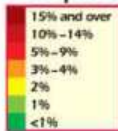
**STEP 3: Compare Predicted 10 year Absolute Risk with "Average" and "Ideal" 10 year Risks, to give Relative Risks**

Age	30 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	65 - 69	70 - 74
"Average" Male	3%	5%	7%	11%	14%	16%	21%	25%	30%
"Ideal" Male	2%	3%	4%	4%	6%	7%	9%	11%	14%
"Average" Female	< 1%	< 1%	2%	5%	8%	12%	12%	13%	14%
"Ideal" Female	< 1%	1%	2%	3%	5%	7%	8%	8%	8%

"Ideal" risk represents
Total Cholesterol = 4.1 - 5.1
HDL = 1.2 (Male), 1.4 (Female)
BP < 120/80
No Diabetes, Non Smoker

People with an absolute risk of ≥20% should be considered for treatment: with a Statin to achieve a Total Cholesterol <5 and/or LDL cholesterol <3.2 with anti-hypertensives to achieve a BP ≤160/90 (ideally ≤140/80)

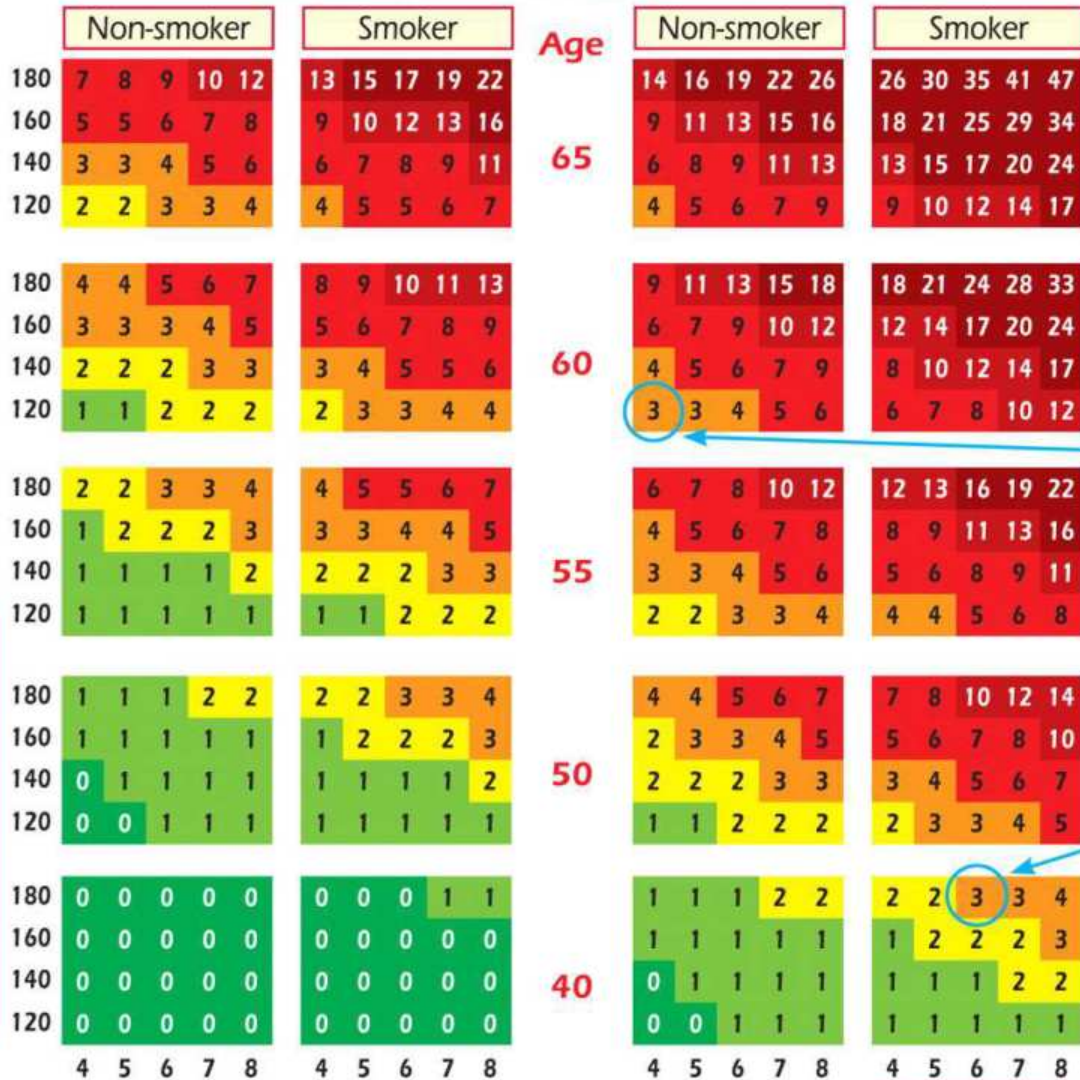
SCORE



10-year risk of fatal CVD in populations at high CVD risk

WOMEN

MEN



The risk of this 40 year old male smoker with risk factors is the same (3%) as that of a 60 year old man with ideal risk factor levels—therefore his risk age is 60 years.

Systolic blood pressure (mmHg)

Total cholesterol (mmol/L)

150 200 250 300 mg/dL

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- Diabetes mellitus YOK
- Belirgin tek bir risk faktörü (ör Dislipidemi veya hipertansiyon) YOK
- Böbrek fonksiyon problemi YOK (GFR>60 mL/dk)
- SCORE  $\leq$  %1 veya Framingham skoru  $\leq$  5 (10 yıllık KVH)
- [www.HeartScore.org](http://www.HeartScore.org)
- <http://cvdrisk.nhlbi.nih.gov/>

# WHI Estrogen+Progestin Trial Study Results - Cardiovascular

