

DIYABET TEDAVİSİNDE HEDEF KAN BASINCI:

Hedef ne olmalı?

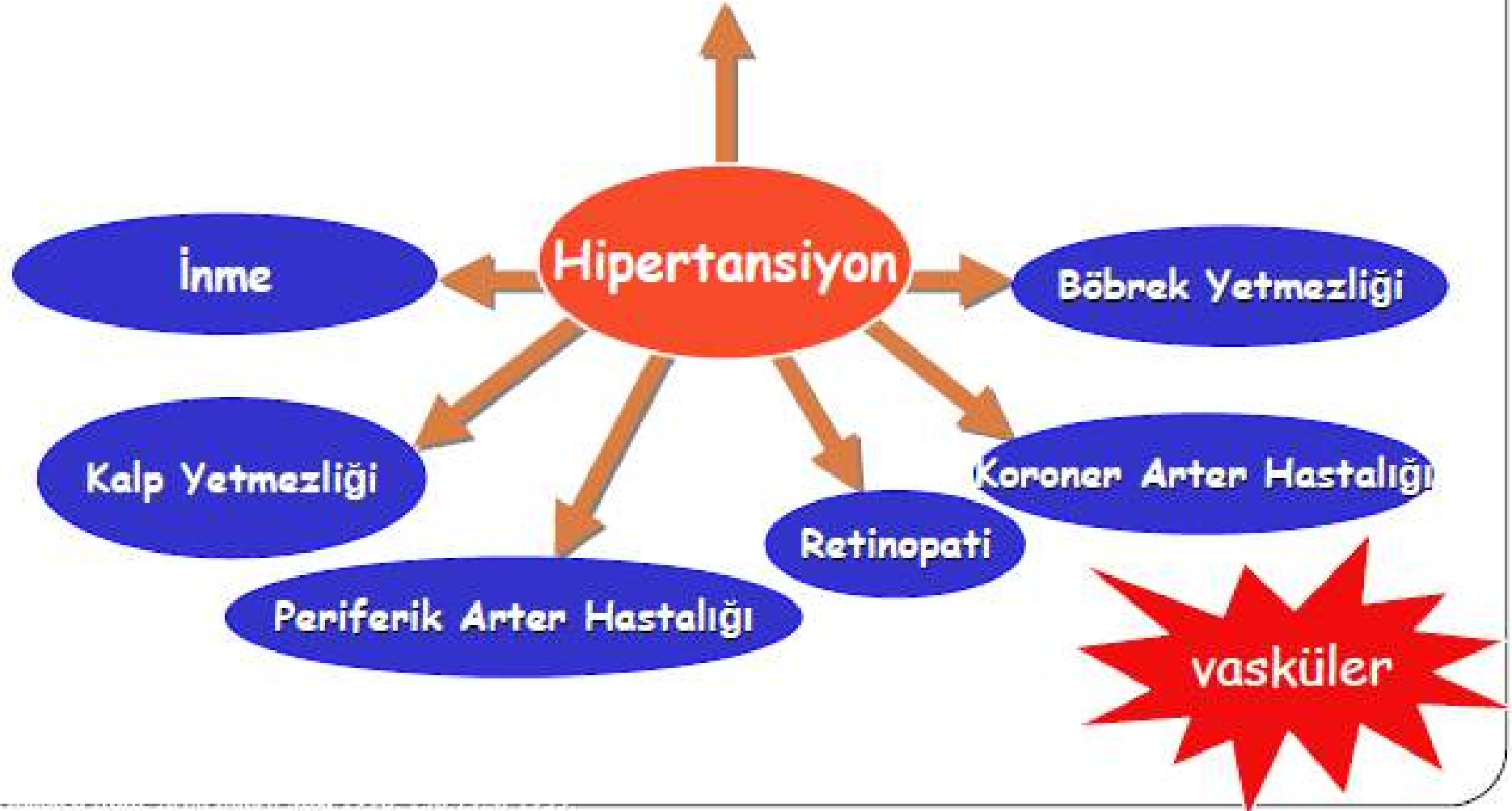
İntensif tedavi gereklimi?

PROF.DR.TEVFİK SABUNCU

Harran Üniversitesi, Tıp Fakültesi

Endokrinoloji Bilim Dalı

Kontrol altına alınabilir,
önlenebilir



2003 JNC-VII Hipertansiyon Sınıflandırması

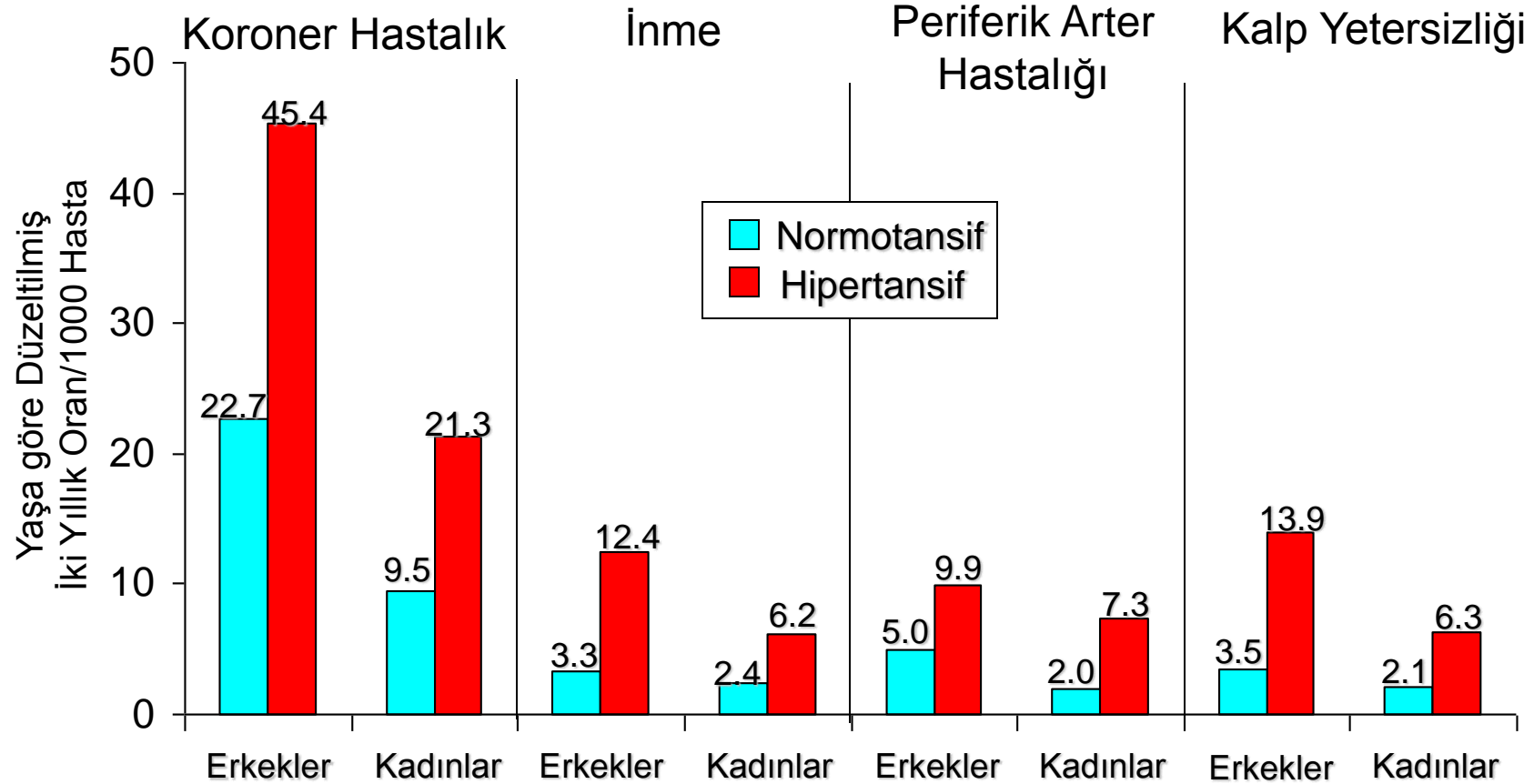
	Sistolik KB	Diastolik KB
Normal	< 120	< 80
Prehipertansiyon	120 - 139	80 - 89
Evre 1 HT	140 - 159	90 - 99
Evre 2 HT	> 160	> 100

2013 ESH - ESC Hipertansiyon Sınıflandırması

	Sistolik KB	Diastolik KB
Optimal	<120	<80
Normal	120 - 129	80 - 84
Yüksek normal	130 - 139	85 - 89
Evre 1 HT	140 - 159	90 - 99
Evre 2 HT	160 - 179	100 - 109
Evre 3 HT	>180	>110
İzole sistolik HT	>140	< 90

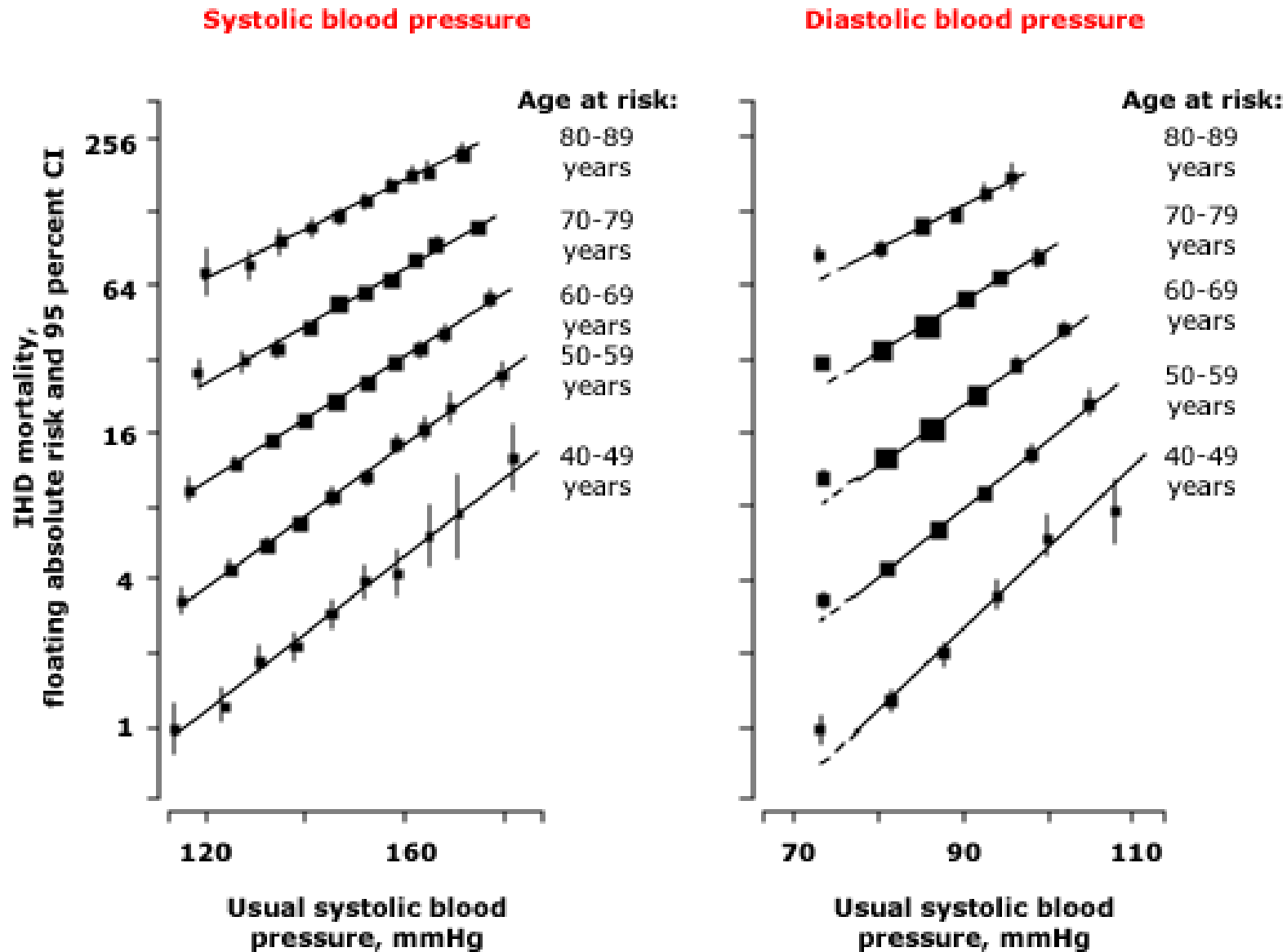
HİPERTANSİF HASTALAR KARDİYOVASKÜLER OLAYLAR AÇISINDAN ARTMIŞ RİSK ALTINDADIR

Framingham Çalışması

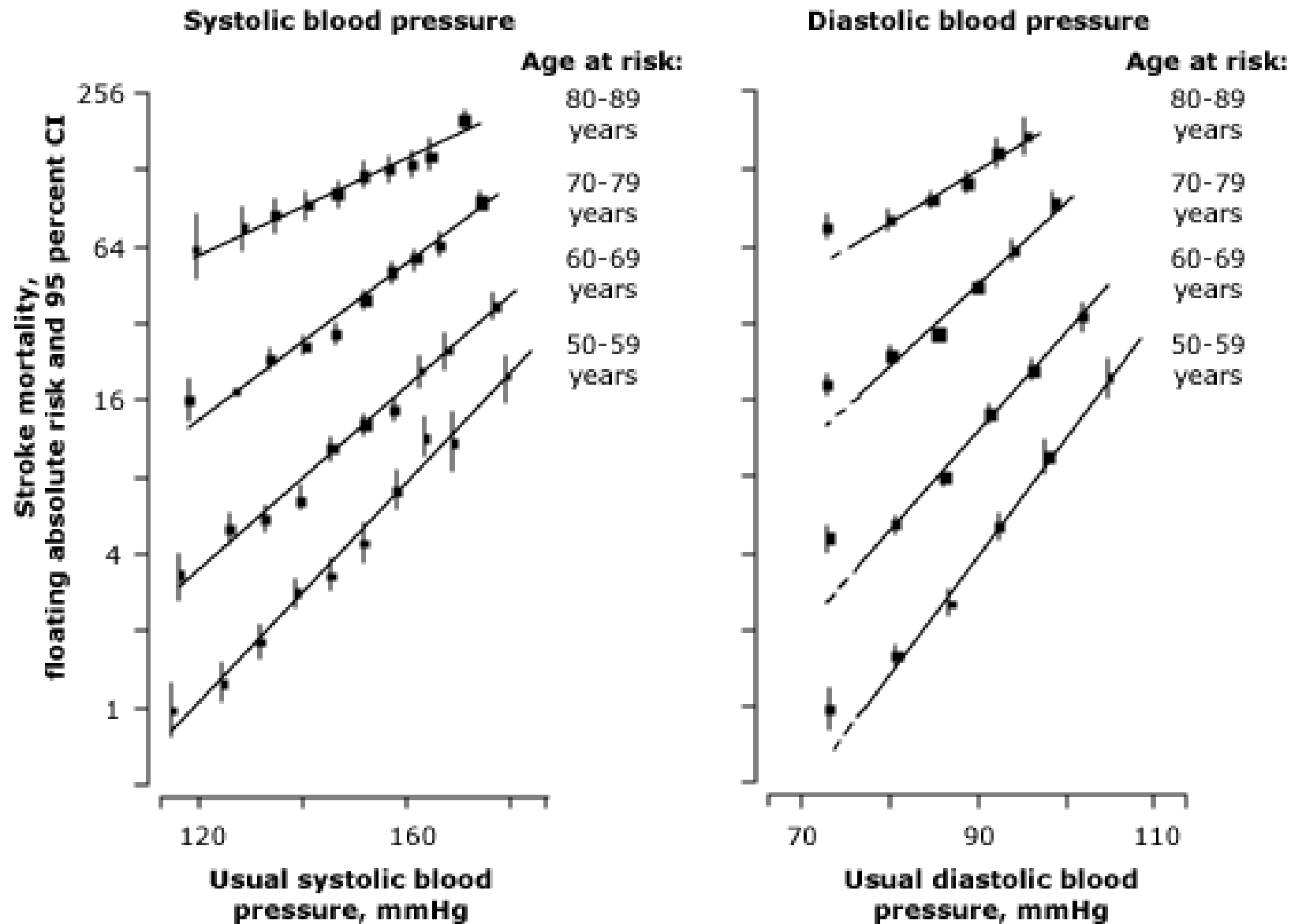


35-64 arası yaştaki hastalarda 36 yıllık takip

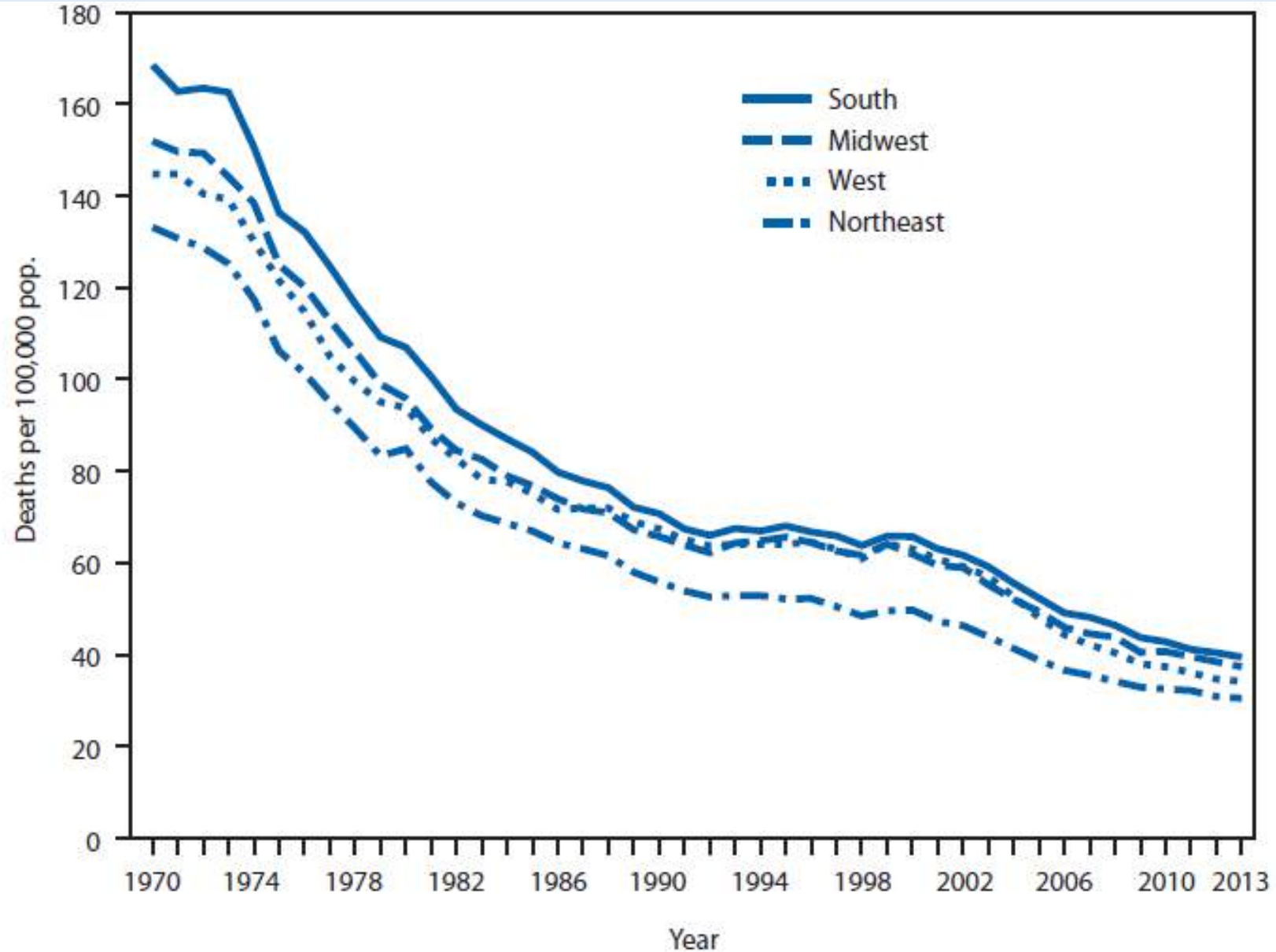
Kan basıncı ve yaşa göre KKH mortalite riski



Kan basıncı ve yaşa göre inme mortalite riski



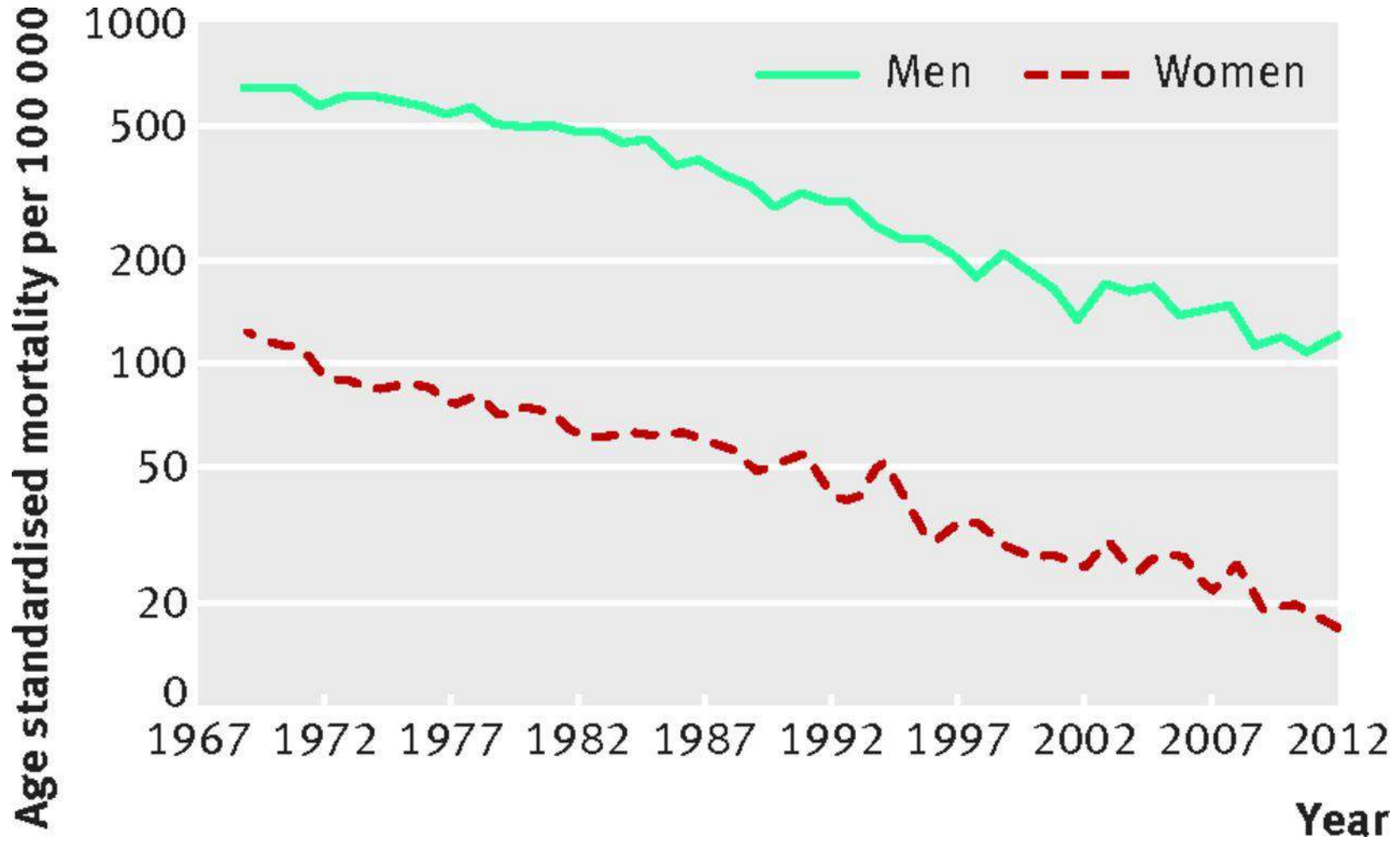
ABD'de Yıllar içinde azalan İnme Mortalite Oranları



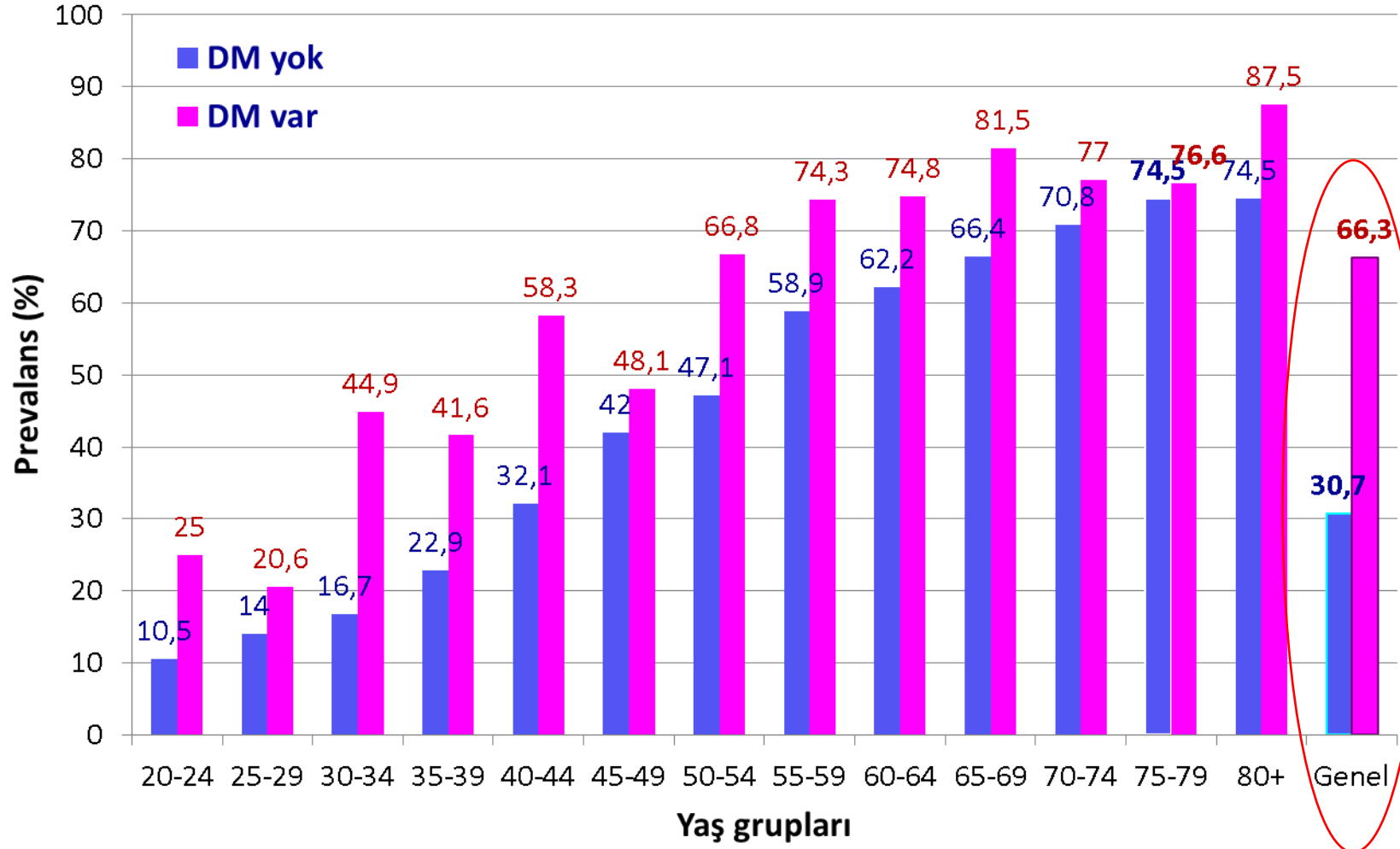
JAMA. 2015;314(16):1731-1739

www.cdc.gov/mmwr/preview/mmwrhtml/mm6413a9.htm

Finlandiya'da Yıllar içinde azalan KKH Mortalite Oranları (1969-2012, 35-64 yaş)



TURDEP-I: Diyabeti olan ve olmayan bireylerde hipertansiyon



1998: DM'lilerde HT 2.2 kat daha yüksek!..

UKPDS-Sıkı ve az sıkı KB kontrolü yapılanlarda sağlanan KB değerleri

1148 HT tip-2 DM'li hasta

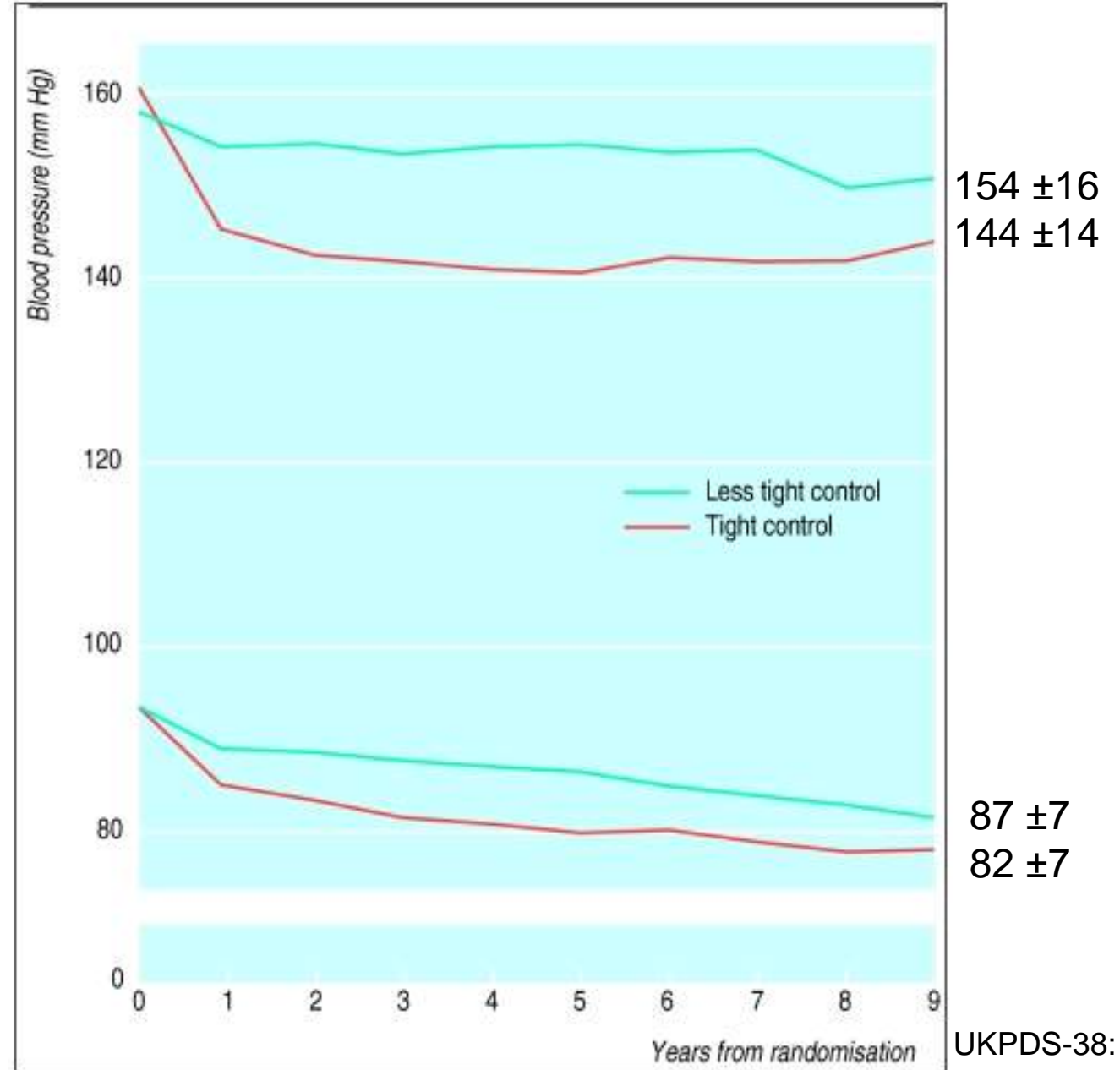
Sıkı KB kontrol hedefi: <150/85 mm Hg

Az Sıkı KB kontrol hedefi: <180/105 mm Hg

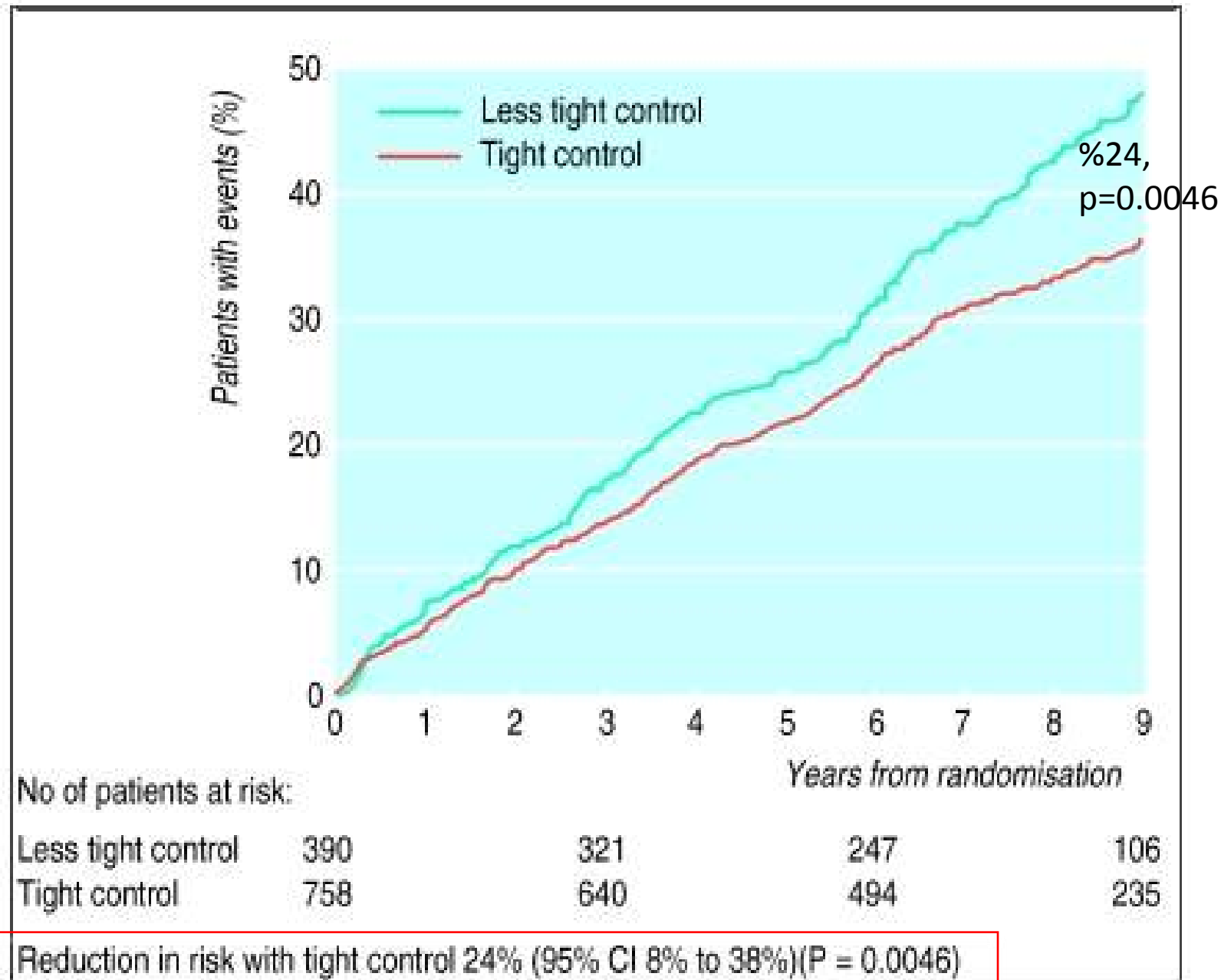
Sağlanan KB değerleri:

Sıkı grupta: 144 (± 14)/82 (± 7) mm Hg

Az sıkı grupta: 154 (± 16)/87 (± 7) mm Hg

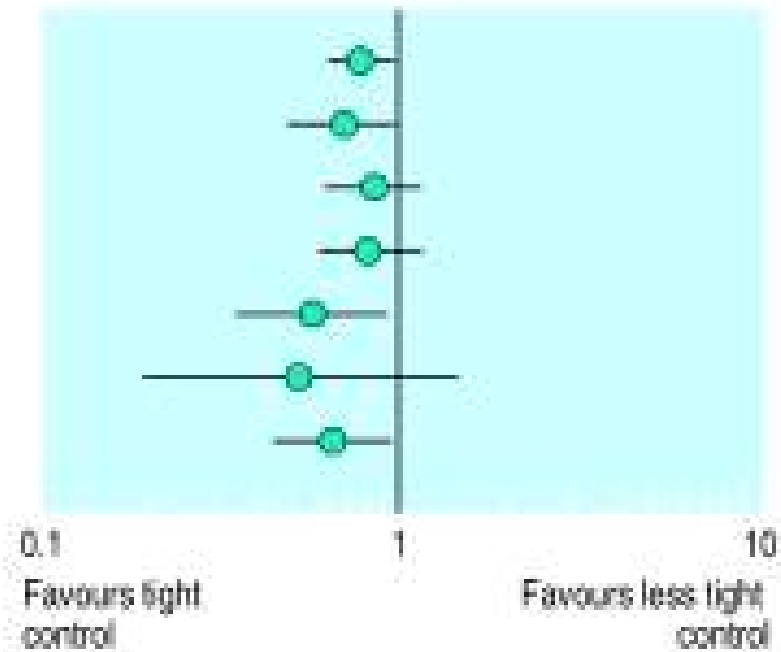


UKPDS-Sıkı KB kontrolü uygulananlarda olay oranı

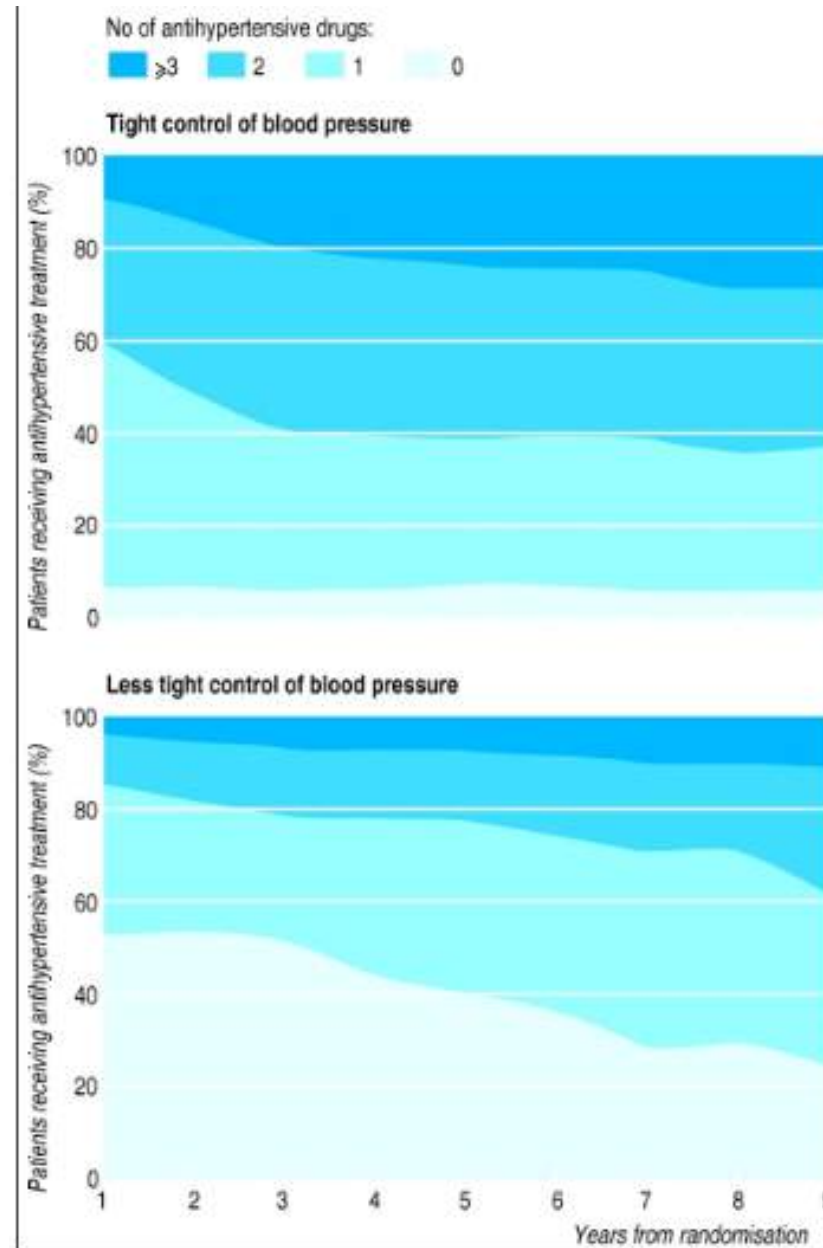


UKPDS-Sıkı KB kontrolü uygulananlarda klinik son noktalar

Clinical end point	Patients with aggregate end points		Absolute risk (events per 1000 patient years)		P value	Relative risk for tight control (95% CI)
	Tight control (n=758)	Less tight control (n=390)	Tight control	Less tight control		
Any diabetes related end point	259	170	50.9	67.4	0.0048	0.76 (0.62 to 0.92)
Deaths related to diabetes	82	62	13.7	20.3	0.019	0.58 (0.49 to 0.94)
All cause mortality	134	83	22.4	27.2	0.17	0.82 (0.63 to 1.08)
Myocardial infarction	107	69	18.6	23.5	0.13	0.79 (0.59 to 1.07)
Stroke	38	34	6.5	11.6	0.013	0.56 (0.35 to 0.89)
Peripheral vascular disease	8	8	1.4	2.7	0.17	0.51 (0.19 to 1.37)
Microvascular disease	68	54	12.0	19.2	0.0092	0.63 (0.44 to 0.89)



Sıkı KB kontrolü daha fazla ilaç kullanımını gerektirir

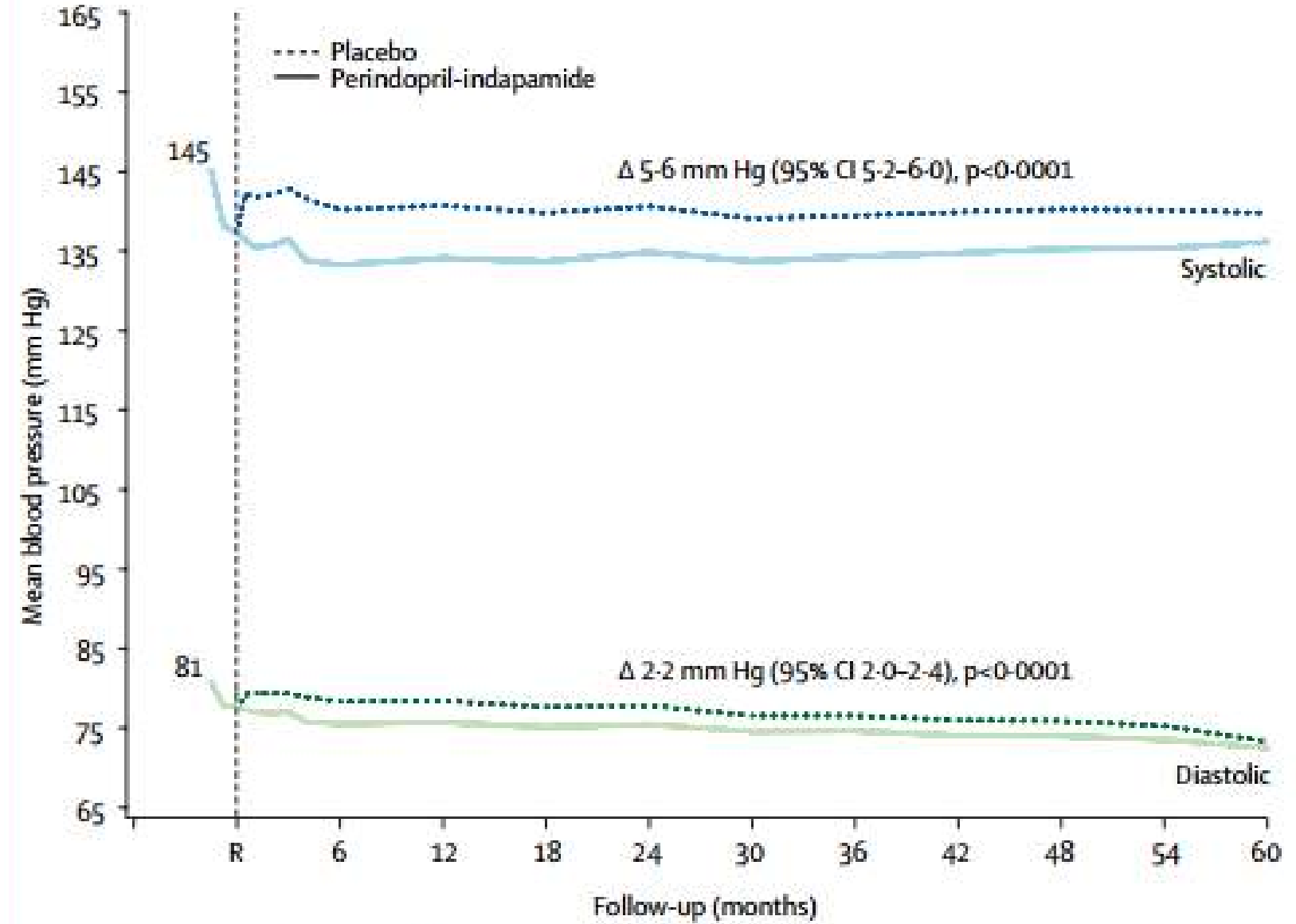


HOT Çalışması- Tedavi Gruplarında Kümülatif Riskler

Event	Number of events	Events/1000 patient-years	p for trend	Comparison	Relative risk (95% CI)
Major cardiovascular events					
≤90 mm Hg	45	24.4		90 vs 85	1.32 (0.84-2.06)
≤85 mm Hg	34	18.6		85 vs 80	1.56 (0.91-2.67)
≤80 mm Hg	22	11.9	0.005	90 vs 80	2.06 (1.24-3.44)
Major cardiovascular events, including silent myocardial infarction					
≤90 mm Hg	48	26.2		90 vs 85	1.13 (0.75-1.71)
≤85 mm Hg	42	23.3		85 vs 80	1.42 (0.89-2.26)
≤80 mm Hg	30	16.4	0.045	90 vs 80	1.60 (1.02-2.53)
All myocardial infarction					
≤90 mm Hg	14	7.5		90 vs 85	1.75 (0.73-4.17)
≤85 mm Hg	8	4.3		85 vs 80	1.14 (0.41-3.15)
≤80 mm Hg	7	3.7	0.11	90 vs 80	2.01 (0.81-4.97)
All myocardial infarction, including silent cases					
≤90 mm Hg	18	9.7		90 vs 85	1.12 (0.57-2.19)
≤85 mm Hg	16	8.7		85 vs 80	1.07 (0.53-2.16)
≤80 mm Hg	15	8.1	0.61	90 vs 80	1.20 (0.60-2.38)
All stroke					
≤90 mm Hg	17	9.1		90 vs 85	1.30 (0.63-2.67)
≤85 mm Hg	13	7.0		85 vs 80	1.10 (0.50-2.40)
≤80 mm Hg	12	6.4	0.34	90 vs 80	1.43 (0.68-2.99)
Cardiovascular mortality					
≤90 mm Hg	21	11.1		90 vs 85	0.99 (0.54-1.82)
≤85 mm Hg	21	11.2		85 vs 80	3.0 (1.29-7.13)
≤80 mm Hg	7	3.7	0.016	90 vs 80	3.0 (1.28-7.08)
Total mortality					
≤90 mm Hg	30	15.9		90 vs 85	1.03 (0.62-1.71)
≤85 mm Hg	29	15.5		85 vs 80	1.72 (0.95-3.14)
≤80 mm Hg	17	9.0	0.068	90 vs 80	1.77 (0.98-3.21)

%50 daha düşük

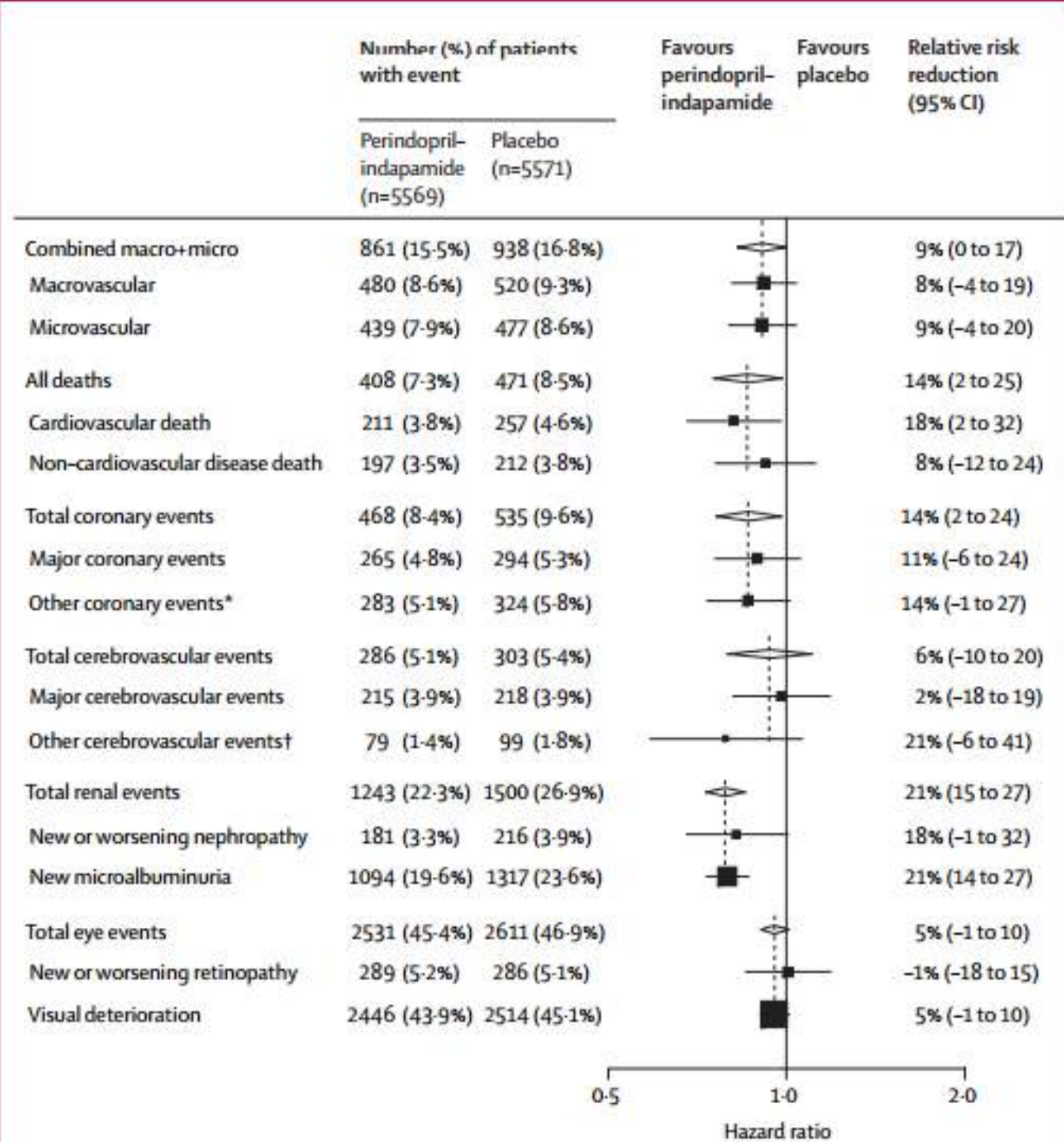
ADVANCE Çalışması- Grupların Kan Basıncı Değerleri



Placebo	137/78	140/78	141/78	140/78	141/78	139/77	139/77	140/76	140/76	140/75	140/73
Per-ind	137/78	133/76	134/76	134/75	135/75	134/75	134/75	135/74	135/74	135/74	136/73

ADVANCE Çalışması- Tedavi Gruplarında Kümülatif Riskler

Aktif tedavi iyi tolere edilmiş,
4.3 yıllık çalışma sonunda tedaviye bağlılık oranları;
A:%73, P:%74



P<0.05

P<0.05

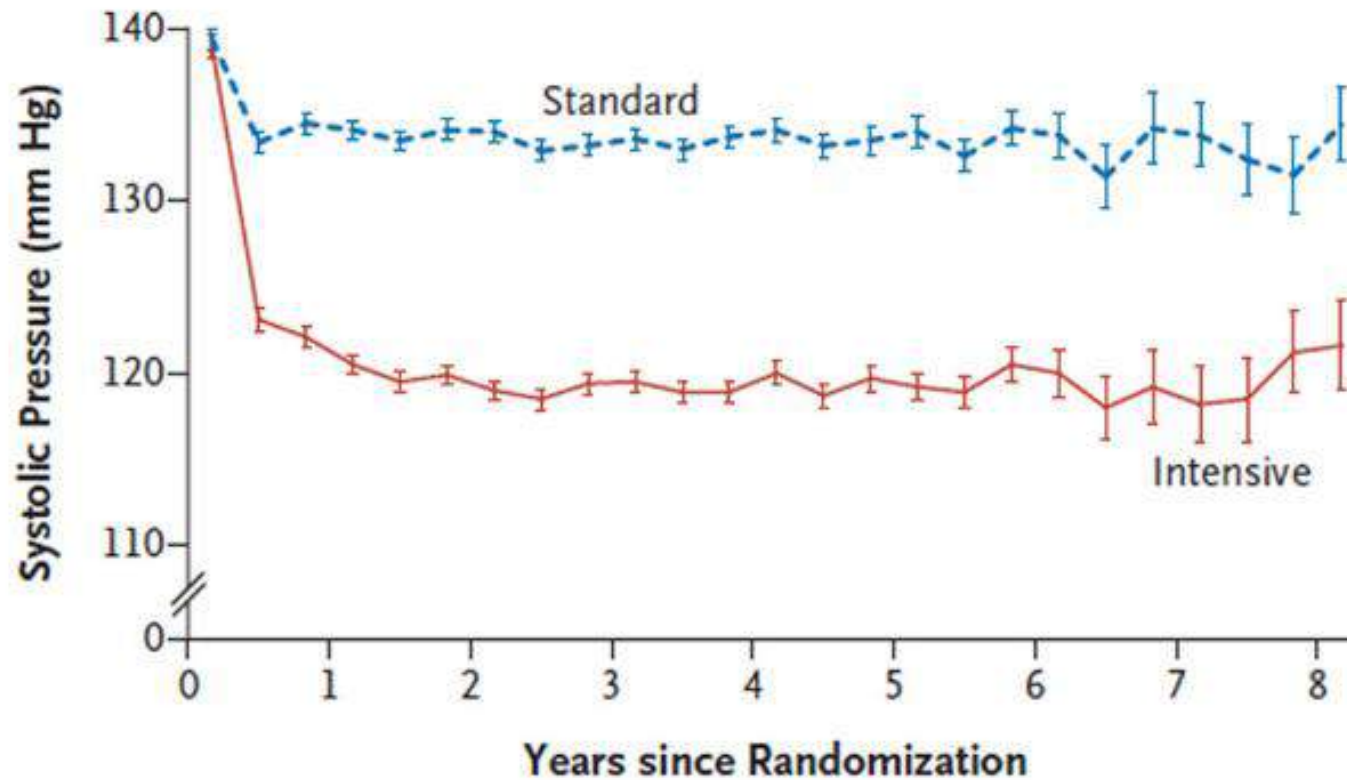
P<0.05

P>0.05

P<0.001

P>0.05

ACCORD Çalışması-Tedavi Gruplarında SKB Düzeyleri



Mean No. of Medications Prescribed

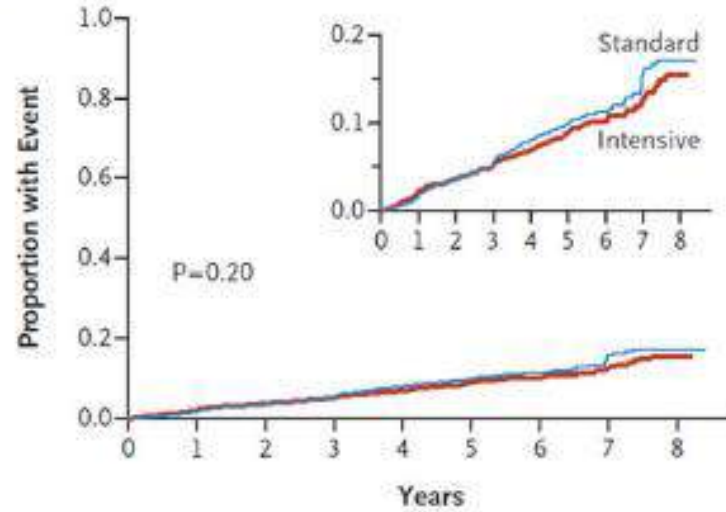
Intensive	3.2	3.4	3.4	3.5	3.5	3.5	3.4	3.4
Standard	1.9	2.1	2.1	2.2	2.2	2.3	2.3	2.3

No. of Patients

Intensive	2174	2071	1973	1792	1150	445	156	156
Standard	2208	2136	2077	1860	1241	504	203	201

ACCORD Çalışması- Tedavi Gruplarında Kümülatif Riskler

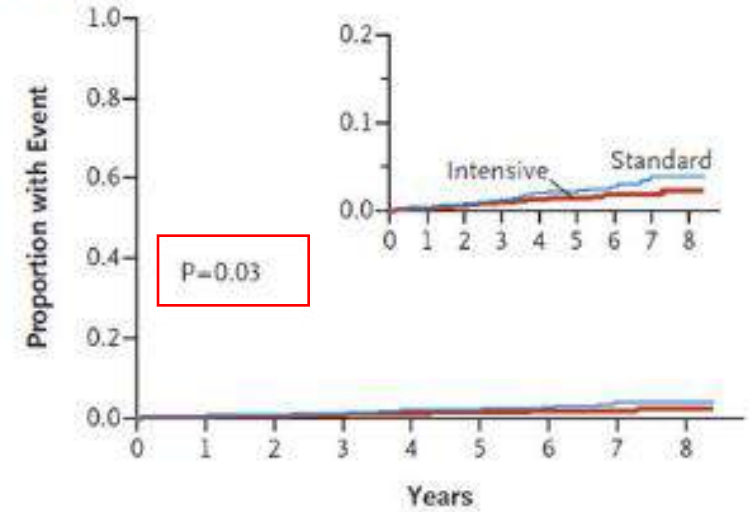
A Primary Outcome



No. at Risk

Intensive	2362	2273	2182	2117	1770	1080	298	175	80
Standard	2371	2274	2196	2120	1793	1127	358	195	108

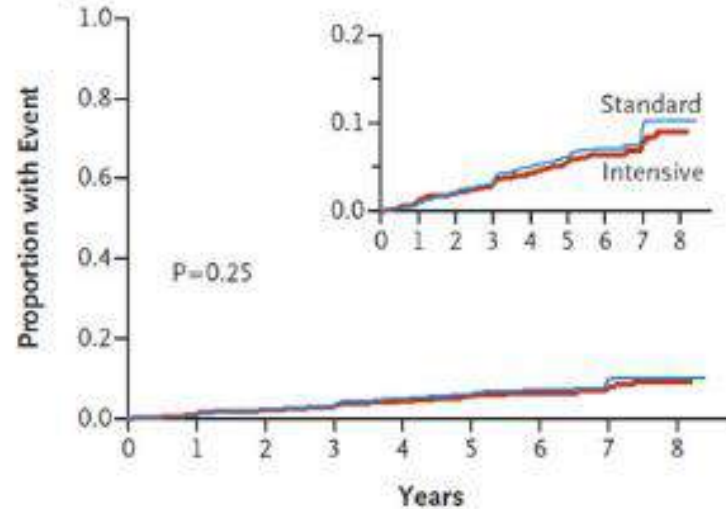
B Nonfatal Stroke



No. at Risk

Intensive	2362	2291	2223	2174	1841	1128	313	186	88
Standard	2371	2287	2235	2186	1879	1196	382	215	114

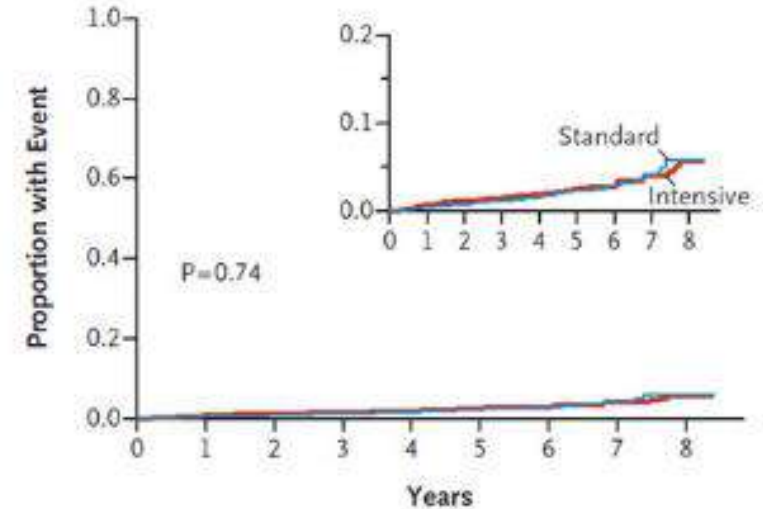
C Nonfatal Myocardial Infarction



No. at Risk

Intensive	2362	2278	2190	2133	1787	1087	299	177	82
Standard	2371	2278	2208	2141	1818	1145	365	201	112

D Death from Cardiovascular Disease



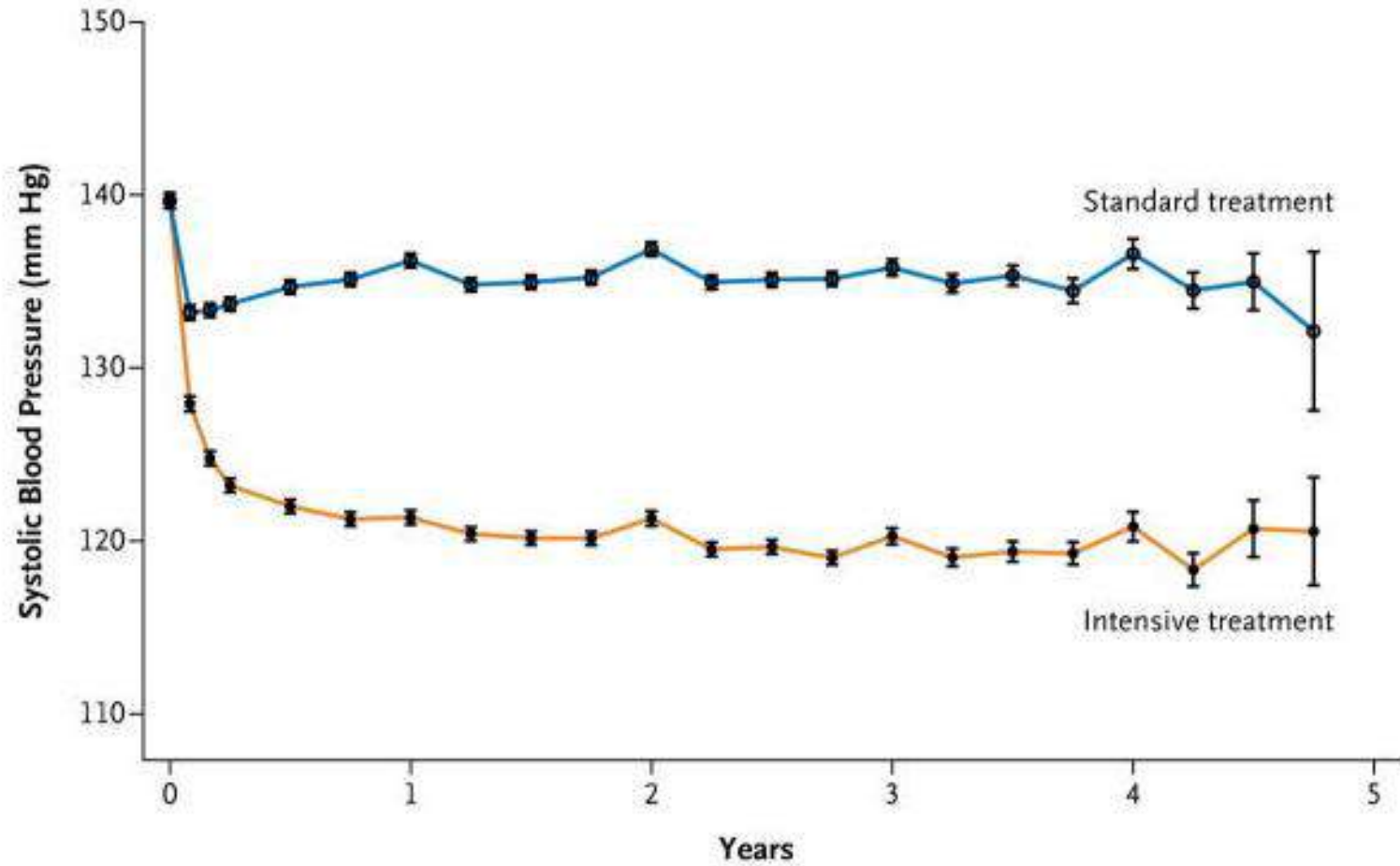
No. at Risk

Intensive	2362	2304	2252	2201	1870	1143	317	188	91
Standard	2371	2313	2268	2218	1922	1220	393	221	118

ACCORD Çalışması-Tedavi Gruplarında Yan etki Oranları

Variable	Intensive Therapy (N = 2362)	Standard Therapy (N = 2371)	P Value
Serious adverse events — no. (%)[‡]			
Event attributed to blood-pressure medications	77 (3.3)	30(1.27)	<0.001
Hypotension	17 (0.7)	1 (0.04)	<0.001
Syncope	12 (0.5)	5 (0.21)	0.10
Bradycardia or arrhythmia	12 (0.5)	3 (0.13)	0.02
Hyperkalemia	9 (0.4)	1 (0.04)	0.01
Angioedema	6 (0.3)	4(0.17)	0.55
Renal failure	5 (0.2)	1 (0.04)	0.12
End-stage renal disease or need for dialysis	59 (2.5)	58 (2.4)	0.93

SPRINT Çalışması-Tedavi Gruplarında SKB Düzeyleri



No. with Data

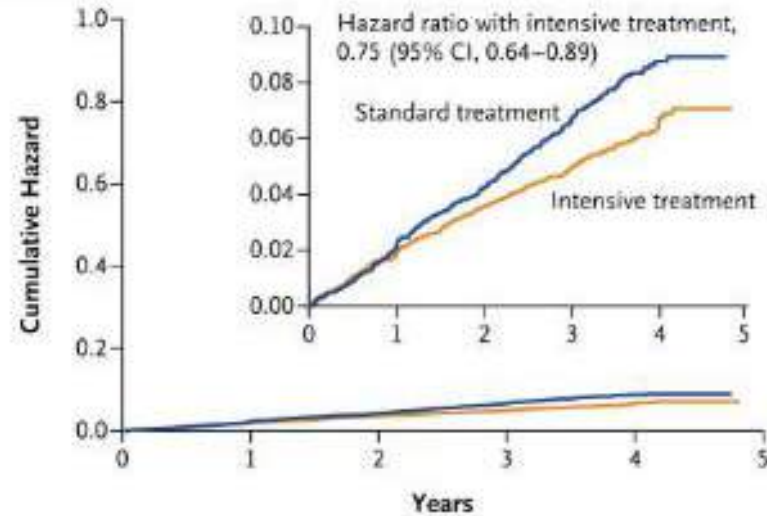
Standard treatment	4683	4345	4222	4092	3997	3904	3115	1974	1000	274
Intensive treatment	4678	4375	4231	4091	4029	3920	3204	2035	1048	286

Mean No. of Medications

Standard treatment	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Intensive treatment	2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0

SPRINT Çalışması- Tedavi Gruplarında Kümülatif Riskler

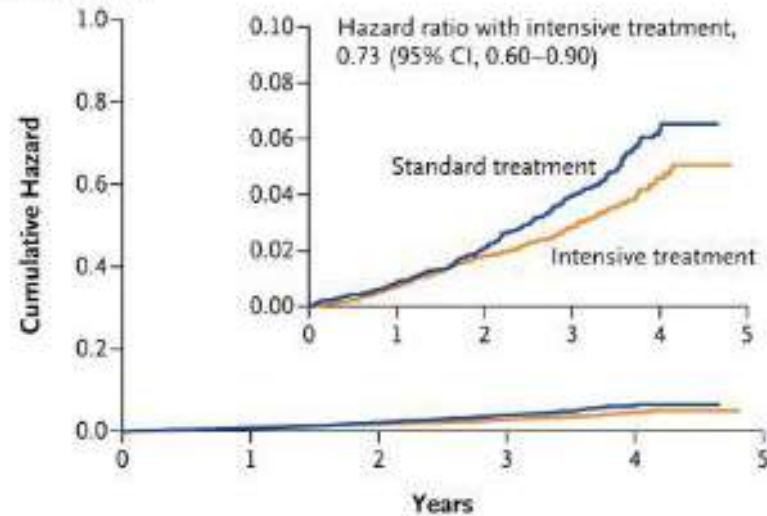
A Primary Outcome



No. at Risk

Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

B Death from Any Cause



No. at Risk

Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

SPRINT Çalışması-Tedavi Gruplarında Kümülatif Riskler

Primer – Sekonder Sonuçlar

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value
	<i>no. of patients (%)</i>	<i>% per year</i>	<i>no. of patients (%)</i>	<i>% per year</i>		
All participants	(N = 4678)		(N = 4683)			
Primary outcome [†]	243 (5.2)	1.65	319 (6.8)	2.19	0.75 (0.64–0.89)	<0.001
Secondary outcomes						
Myocardial infarction	97 (2.1)	0.65	116 (2.5)	0.78	0.83 (0.64–1.09)	0.19
Acute coronary syndrome	40 (0.9)	0.27	40 (0.9)	0.27	1.00 (0.64–1.55)	0.99
Stroke	62 (1.3)	0.41	70 (1.5)	0.47	0.89 (0.63–1.25)	0.50
Heart failure	62 (1.3)	0.41	100 (2.1)	0.67	0.62 (0.45–0.84)	0.002
Death from cardiovascular causes	37 (0.8)	0.25	65 (1.4)	0.43	0.57 (0.38–0.85)	0.005
Death from any cause	155 (3.3)	1.03	210 (4.5)	1.40	0.73 (0.60–0.90)	0.003
Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67–0.90)	<0.001

SPRINT Çalışması-Tedavi Gruplarında Yanetki Oranları

Variable	Intensive Treatment (N = 4678) <i>no. of patients (%)</i>	Standard Treatment (N = 4683) <i>no. of patients (%)</i>	Hazard Ratio	P Value
Serious adverse event [*]	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall [†]	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure [‡]	193 (4.1)	117 (2.5)	1.66	<0.001

Hipertansiyon Tedavisinin KV Sonuçları: SPRINT + ACCORD

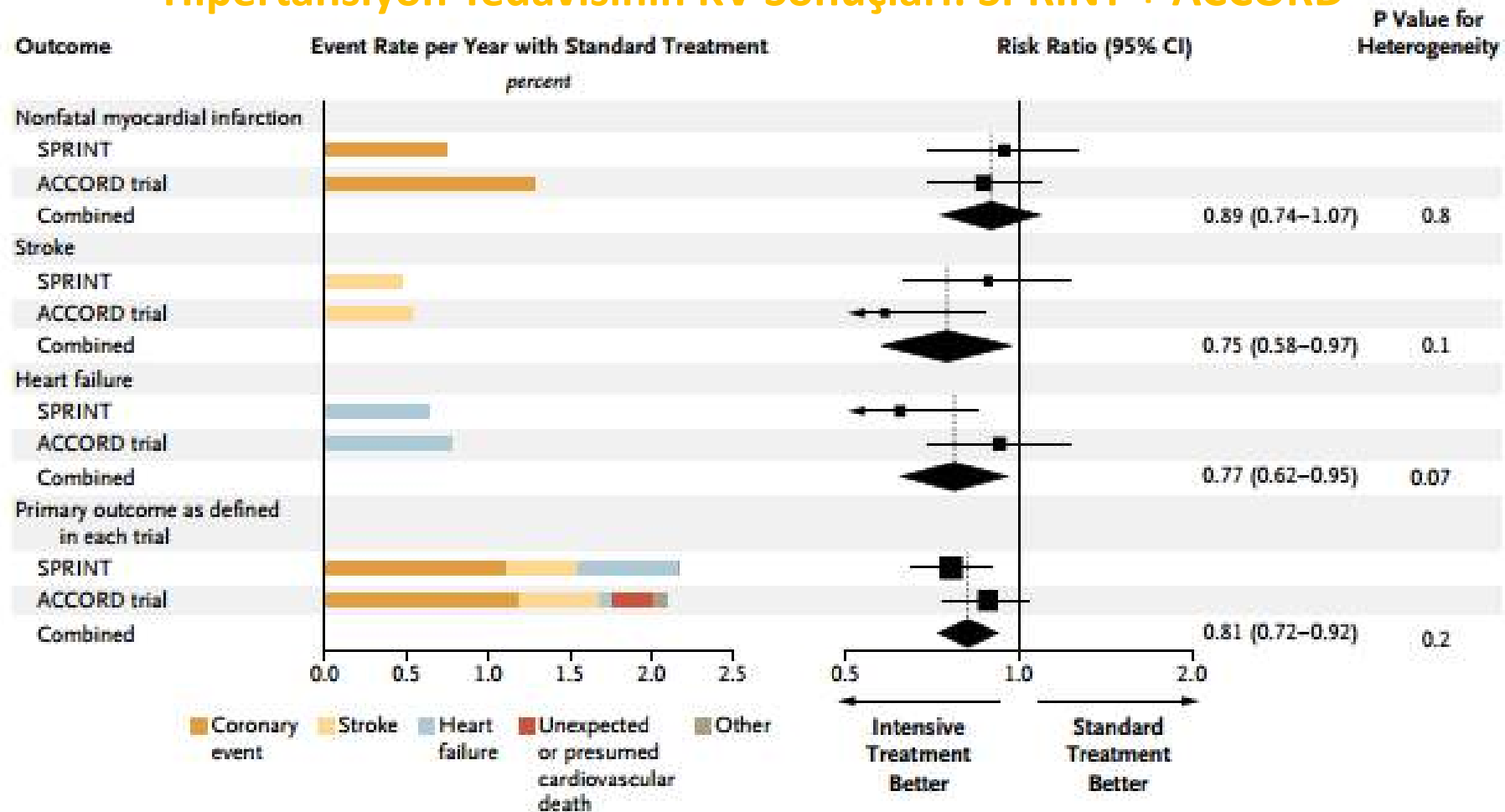
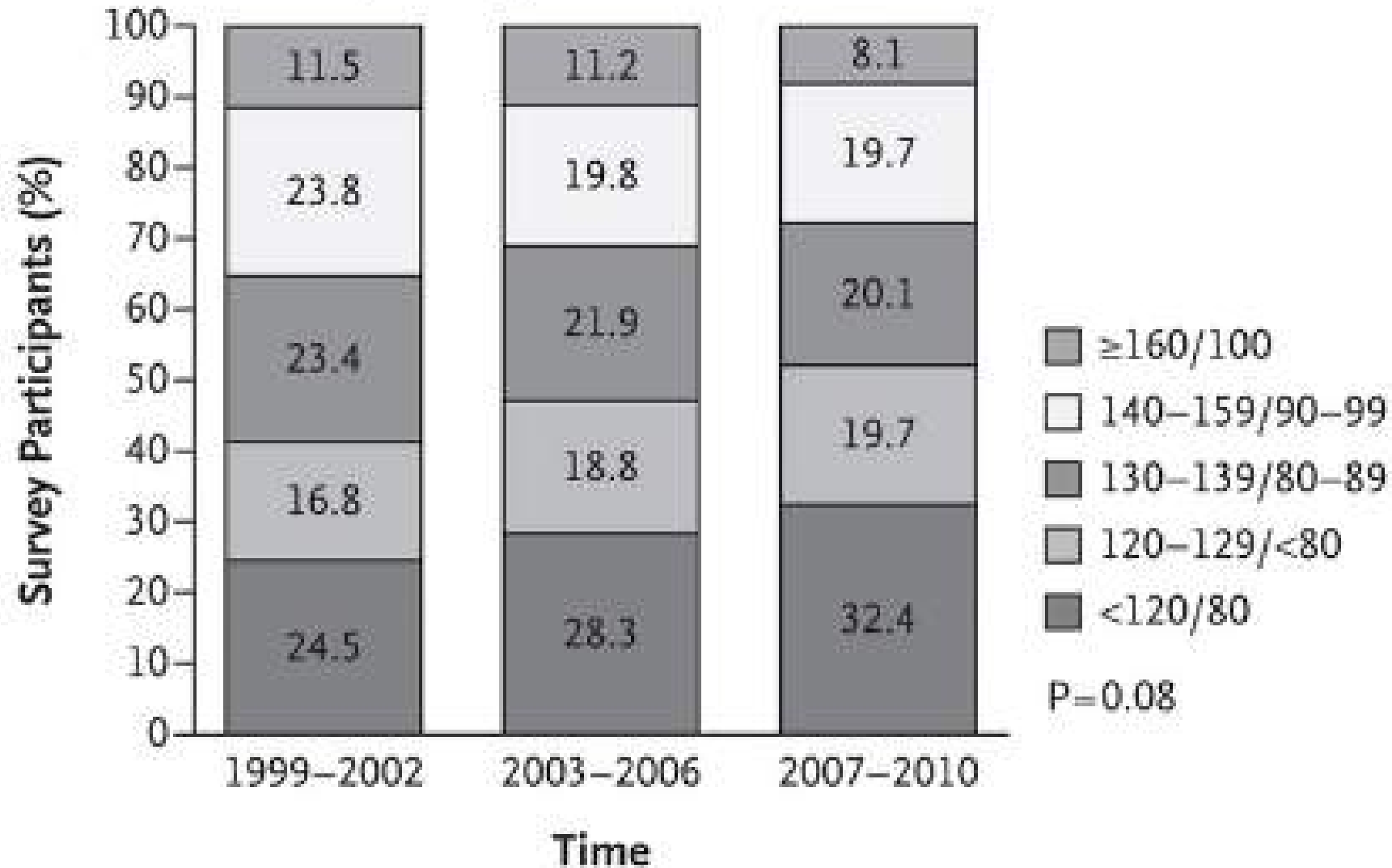


Figure 1. Outcomes Data from SPRINT and the ACCORD Trial and Combined Data from Both Trials.

In both the Systolic Blood Pressure Intervention Trial (SPRINT) and the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, the systolic blood-pressure target in the intensive-treatment group was less than 120 mm Hg, and the target in the standard-treatment group was less than 140 mm Hg. The primary outcome in the ACCORD trial was nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes. The primary outcome in SPRINT also included acute coronary syndrome not resulting in myocardial infarction and nonfatal episodes of heart failure. For the ACCORD trial only, death from cardiovascular causes included "unexpected death presumed to be due to ischemic cardiovascular disease" and "presumed cardiovascular death," which together accounted for 81 (69%) of the deaths from cardiovascular causes in that trial.

Diyabetli kişilerde Zamanla Kan Basıncı düzeylerinde değişim

B Blood Pressure (mm Hg)

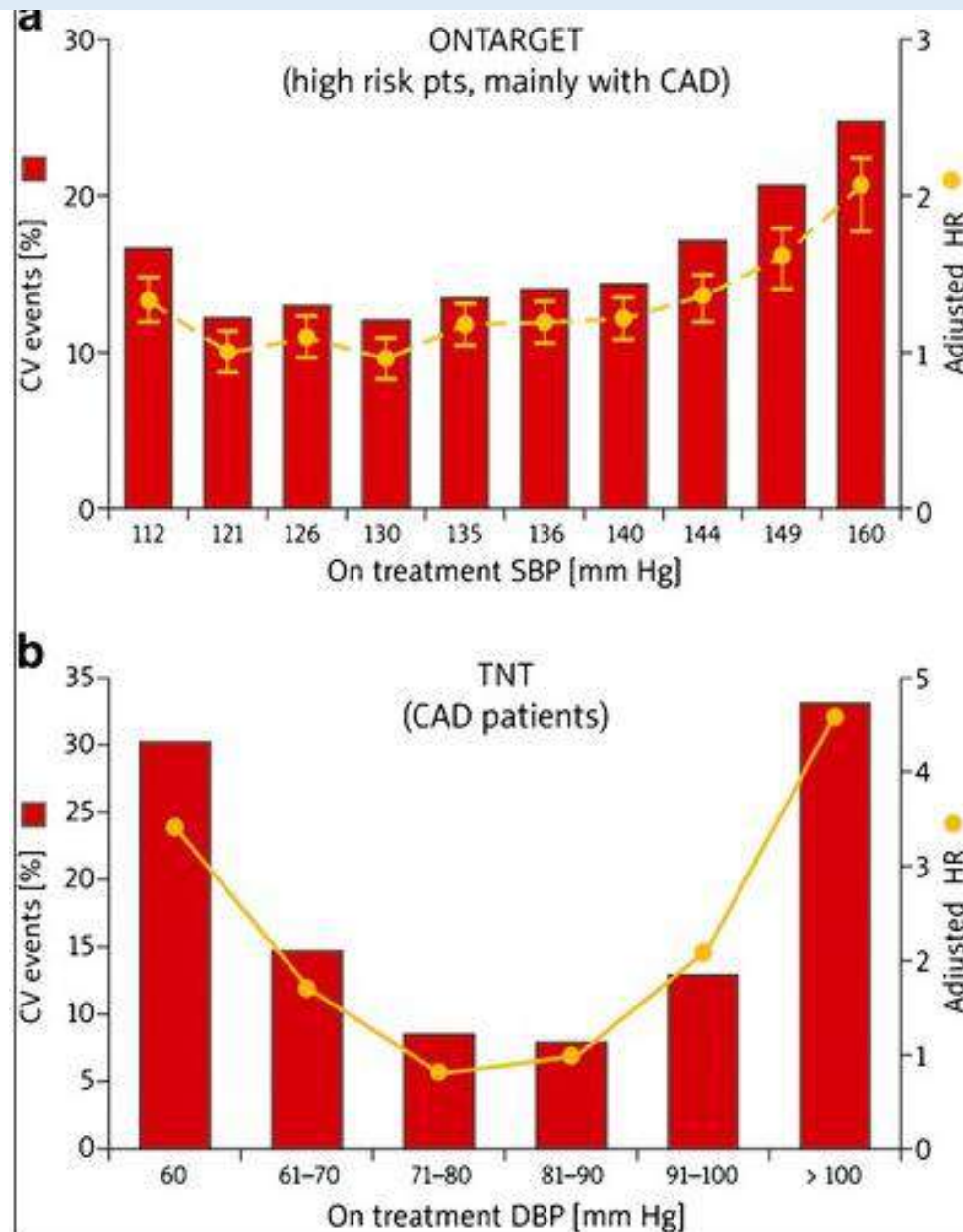


Diyabetli kişilerde Zamanla Risk faktörlerinde sağlanan kontrol oranları

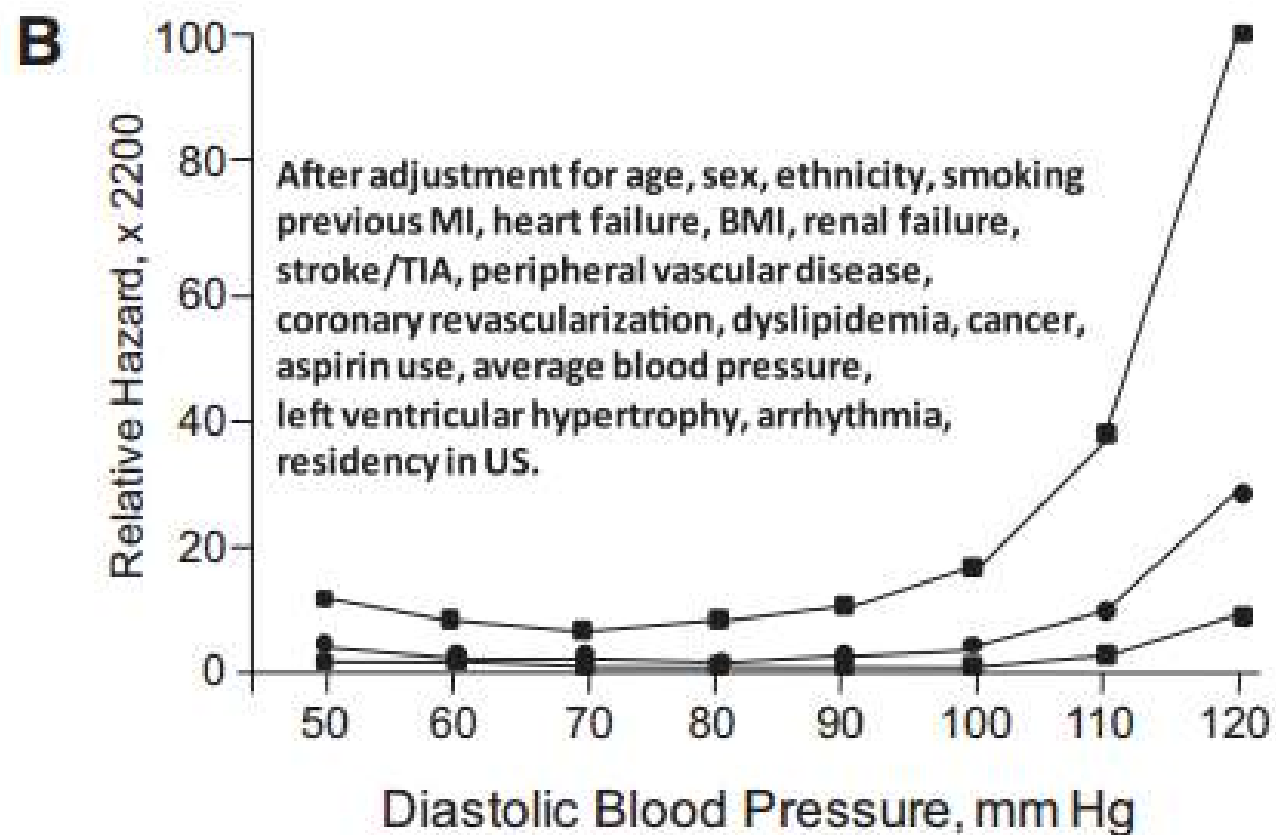
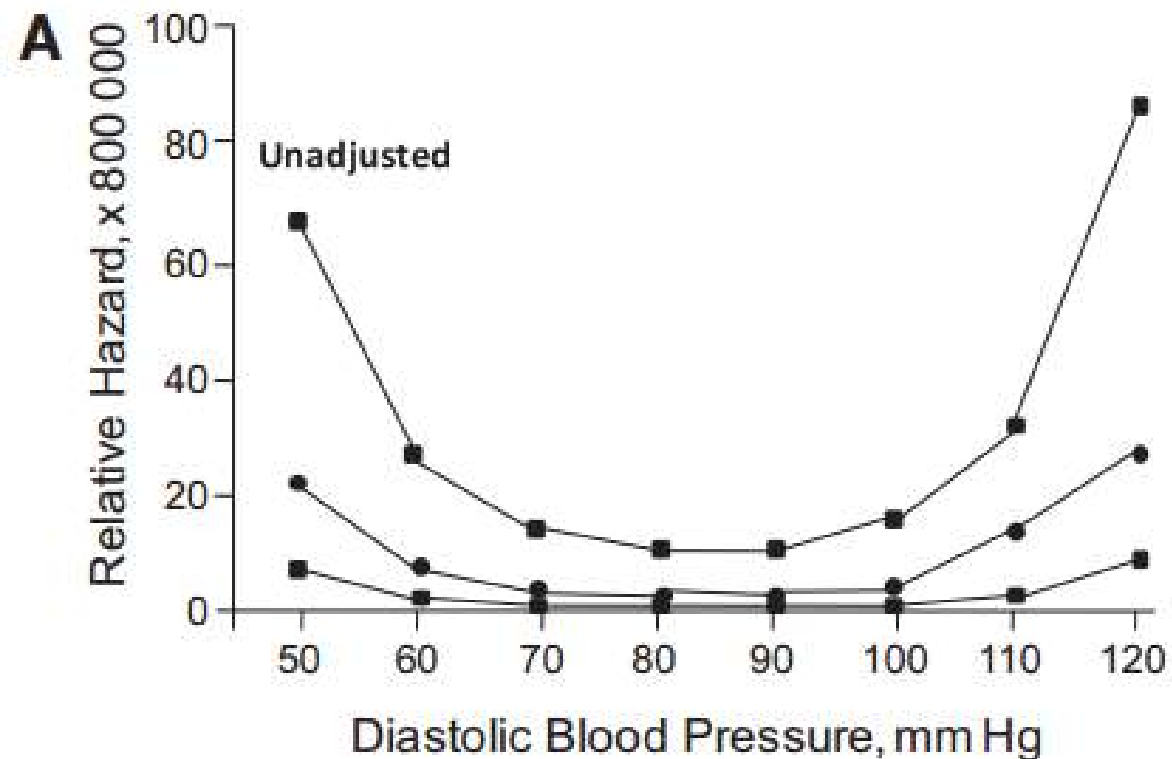
Table 3. Changes in Risk-Factor Control and Adherence to Preventive Practices over Time among U.S. Adults with Diagnosed Diabetes.*

Factor or Practice	% of survey participants			percentage points	
	1999–2002	2003–2006	2007–2010	Change from 1999–2002 to 2007–2010 (95% CI)	Change from 2003–2006 to 2007–2010 (95% CI)
Risk factors					
Glycated hemoglobin					
>9.0%	18.4	13.0	12.6	–5.8 (–10.5 to –1.1)	–0.4 (–3.8 to 3.0)
<8.0%	67.4	78.0	79.1	11.7 (6.3 to 17.1)	1.1 (–3.5 to 5.7)
<7.0%	44.3	56.8	52.2	7.9 (0.8 to 15.0)	–4.6 (–11.1 to 1.9)
Blood pressure <130/80 mm Hg	39.6	45.3	51.3	11.7 (5.7 to 17.7)	6.0 (0.4 to 11.6)
LDL cholesterol†					
<100 mg/dl	36.0	46.6	56.8	20.8 (11.6 to 30.0)	10.2 (2.5 to 17.9)
<70 mg/dl for persons with CVD	15.9	23.2	27.5	11.6 (–4.1 to 27.3)	4.3 (–8.5 to 17.1)
Current smoker, self-reported or cotinine >10 ng/ml	24.0	23.4	22.3	–1.7 (–6.2 to 2.8)	–1.1 (–5.4 to 3.2)
Glycated hemoglobin, blood-pressure, and LDL cholesterol targets and nonsmoking status achieved	4.6	9.5	14.3	9.7 (5.1 to 14.3)	4.8 (–0.4 to 10.0)

J-curve Fenomeni



J-curve Fenomeni



Tip 2 DM'de SKB'nı 10 mmHg düşürmenin sonuçları-Metaanaliz

Figure 2. Standardized Associations Between 10-mm Hg Lower Systolic BP and All-Cause Mortality, Macrovascular Outcomes, and Microvascular Outcomes in Diabetic Patients

Outcome	No. of Studies	BP Lowering		Control		Relative Risk (95% CI)	Favors BP Lowering	Favors Control
		Events	Participants	Events	Participants			
Mortality	20	2334	27693	2319	25864	0.87 (0.78-0.96)		
Cardiovascular disease	17	3230	25756	3280	24862	0.89 (0.83-0.95)		
Coronary heart disease	17	1390	26150	1449	24761	0.88 (0.80-0.98)		
Stroke	19	1350	27614	1475	26447	0.73 (0.64-0.83)		
Heart failure	13	1235	21684	1348	20791	0.86 (0.74-1.00)		
Renal failure	9	596	19835	560	18912	0.91 (0.74-1.12)		
Retinopathy	7	844	9781	905	9566	0.87 (0.76-0.99)		
Albuminuria	7	2799	13804	3163	12821	0.83 (0.79-0.87)		

- Tüm nedenlere bağlı mortaliteyi, KVH'ı, KKH'nı, İnmeyi, Retinopatiyi ve albuminüriyi anlamlı olarak azalttığı, Ancak KY ve KBY riskini azaltamadığı
- Başlangıçtaki SKB düzeylerinden bağımsız olarak tüm çalışmalarda inme ve albuminüri riskini düşürdüğü,
 - Ancak mortalite, KVH, KKH ve KY risklerini sadece başlangıç SKB ≥ 140 mmHg olanlarda anlamlı olarak düşürdüğü,
- Tedavi sonucu KB ≥ 130 mmHg olan hastalarda (KB < 130 mmHg olanlara göre) mortalite, KVH, KKH, KY ve albuminüride daha fazla azalma sağladığı

HT Kılavuzlarının Kan basıncı hedefleri

Kılavuz-Yılı	Kan Basıncı Hedefi (mm Hg)		
	Genel	DM	KBH
JNC 8-2014	<60 yaş: <140/90 ≥60 yaş: <150/90	<140/90	<140/90
ESH/ESC-2013	<140/90 ≥80 yaş: <150/90	<140/85 (Aşık Proteinüri varsa SKB <130)	<140/90
ASH/ISH-2014	<140/90 ≥80 yaş: <150/90	≤140/90	≤140/90 Albuminüri varsa ≤130/80
CHEP-2015	<140/90 ≥80 yaş: <160/90	<130/80	<140/90
KDIGO-2012		Albuminüri yoksa ≤140/90 Albuminüri ≥30 mg/g ise ≤130/80	
NICE-2009 (update:2016)	<80 yaş: <140/90 ≥80 yaş: <150/90	Albuminüri yoksa ≤140/80 Albuminüri ≥30 mg/g ise ≤130/80	
TEMD-2015	<80 yaş: <140/90 ≥80 yaş: <150/90	≤140/90 Genç, Albuminürik, SVH ise <130/80	

ADA-2017 Diyabette Hipertansiyon Önerileri

- Diyabet ve hipertansiyonu olan bireylerde:
KB hedefi: Sistolik <140 mmHg, Diyastolik <90 mmHg olmalı
- Bazı seçilmiş bireylerde (KV riski yüksek hastalar gibi) daha düşük KB <130/80 mmHg hedeflenebilir
- Yaşlılarda:
 - Sağlıklı veya sağlık durumu hafif derecede bozulmuş ise KB hedefi < 140/90 mmHg,
 - Sağlığı ileri derecede bozulmuş, yaşam beklentisi düşük ise KB hedefi <150/90 mmHg
 - Yan etkilere ve polifarmasiye dikkat
- HT ve diyabetli gebe kadınlarda KB hedefleri 120-160/80-105 mmHg olması anne sağlığı ve fetal büyüme geriliği riskini düşürmek açısından ideal kabul edilir

ADA-2017 Diyabette Hipertansiyon Önerileri

- KB $>120/80$ mmHg olan diyabetli hastada yaşam tarzı düzenlenmeli, kilolu ya da obez ise kilo verdirilmelidir
- KB $>140/90$ mmHg olan hastalara yaşam tarzı değişikliğine ek olarak antihipertansif başlanmalı ve hedef değere ulaşana kadar titre edilmeli
- Muayene sırasında doğrulanmış KB $>160/100$ mmHg olan hastalara yaşam tarzı değişikliğine ek olarak ikili antihipertansif başlanmalı ve hedef değere ulaşana kadar titre edilmeli

NETİCE

- Hipertansiyon KVH riskini ciddi biçimde artırmaktadır
- 80 yaş altı tüm diyabetiklerde hedef KB değeri <140/90mmHg
- Diyabetiklerde kan basıncının alt sınırı hususu net değil (Bireyselleştirilmiş tedavi)
- Kardiyovasküler riski yüksek uygun diyabetiklerde SKB < 130mmHg hedeflenebilir
- Koroner perfüzyonu bozmamak için DKB < 60-70mmHg sakınılmalıdır
- İlaç dışı faktörler (tuz, sigara, stres vs) ihmal edilmemelidir
- Tedavinin olası yan etkileri dikkatle izlenmelidir
- Başarılı neticeler için Hekim ve diğer sağlık çalışanlarının, Hasta ve yakınlarının ve SGK ve Hastane yöneticilerinin gayreti ve kaynak temini gereklidir