

A Guidelines-Based Approach to Peripheral Arterial Disease

ARTURO GARCIA TOUCHARD
*Hospital Universitario Puerta de Hierro
Majadahonda*

No disclosures related to presentation

Clinical Presentation

The Spectrum of Manifestations of PAD

- Asymptomatic
- Atypical symptoms
- Intermittent claudication
- Critical limb ischemia
 - Rest Pain
 - Ulceration
 - Necrosis/Gangrene
- Acute limb ischemia

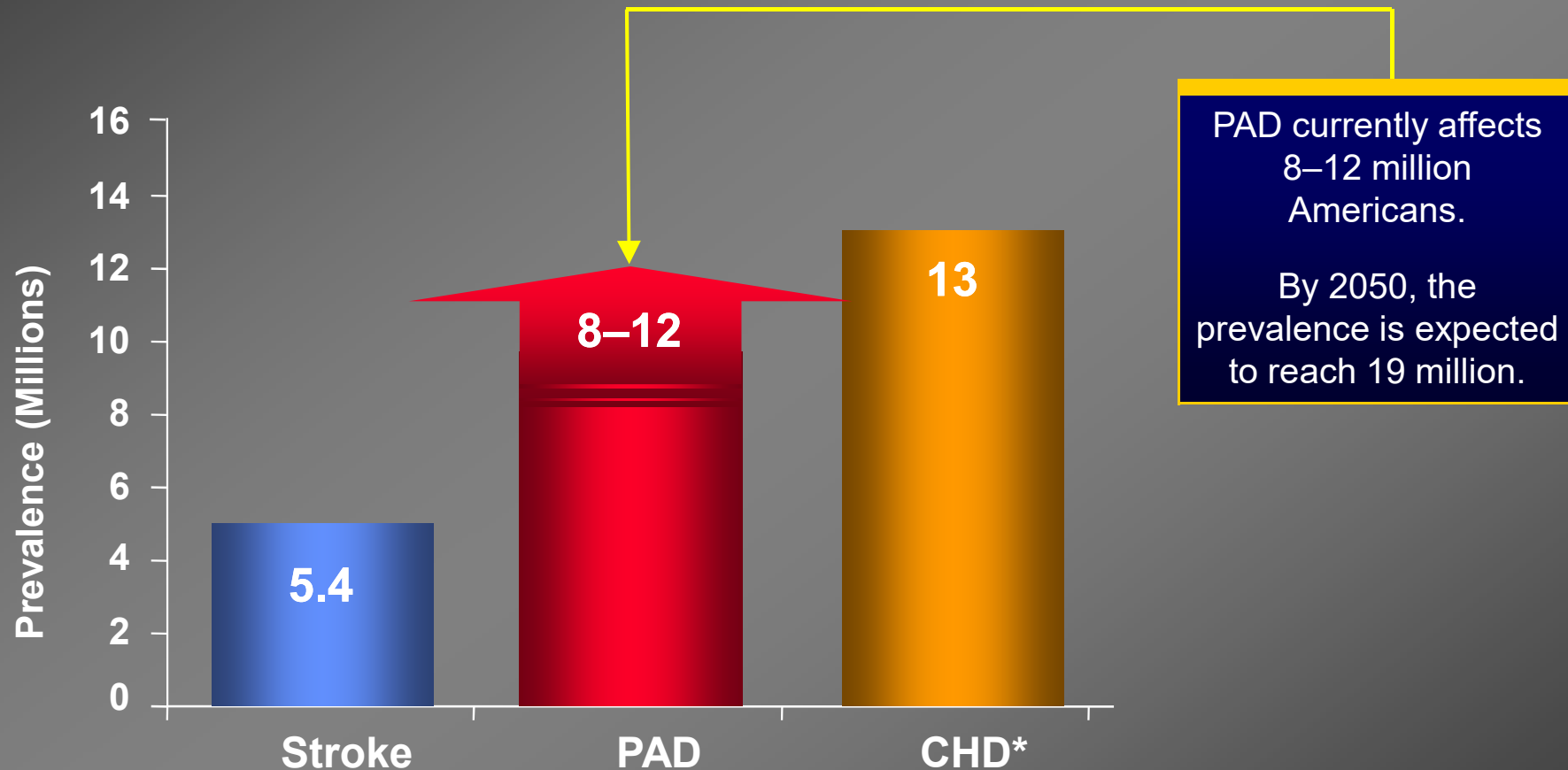


PAD Case #1

- A 74 year old female presents to initiate primary care without complaints
- She has a history of smoking for 40 years, HTN and “borderline” DM
- Medications include clonidine
- Exam reveals BP of 140/86 with non-palpable distal pulses but otherwise no vascular findings
- Labs with LDL of 138 mg/dl and HgA1C of 8.4

Why do we care about her diagnosis of PAD?

Prevalence of PAD in the US

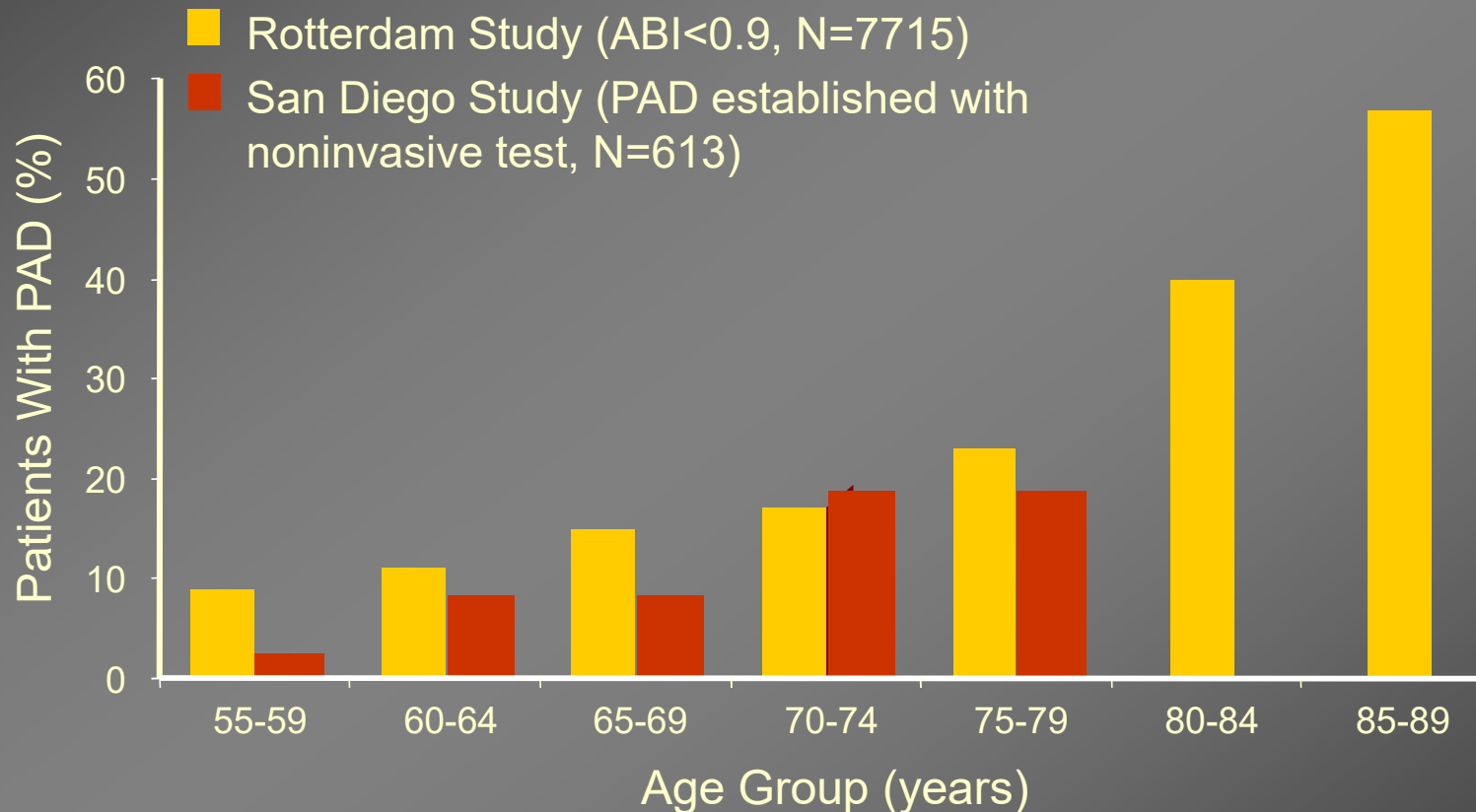


CHD = coronary heart disease. PAD = peripheral arterial disease.

* Includes myocardial infarction and angina pectoris.

American Heart Association. *Heart Disease and Stroke Statistics—2005 Update*. 2005.

Prevalence of PAD Increases With Age



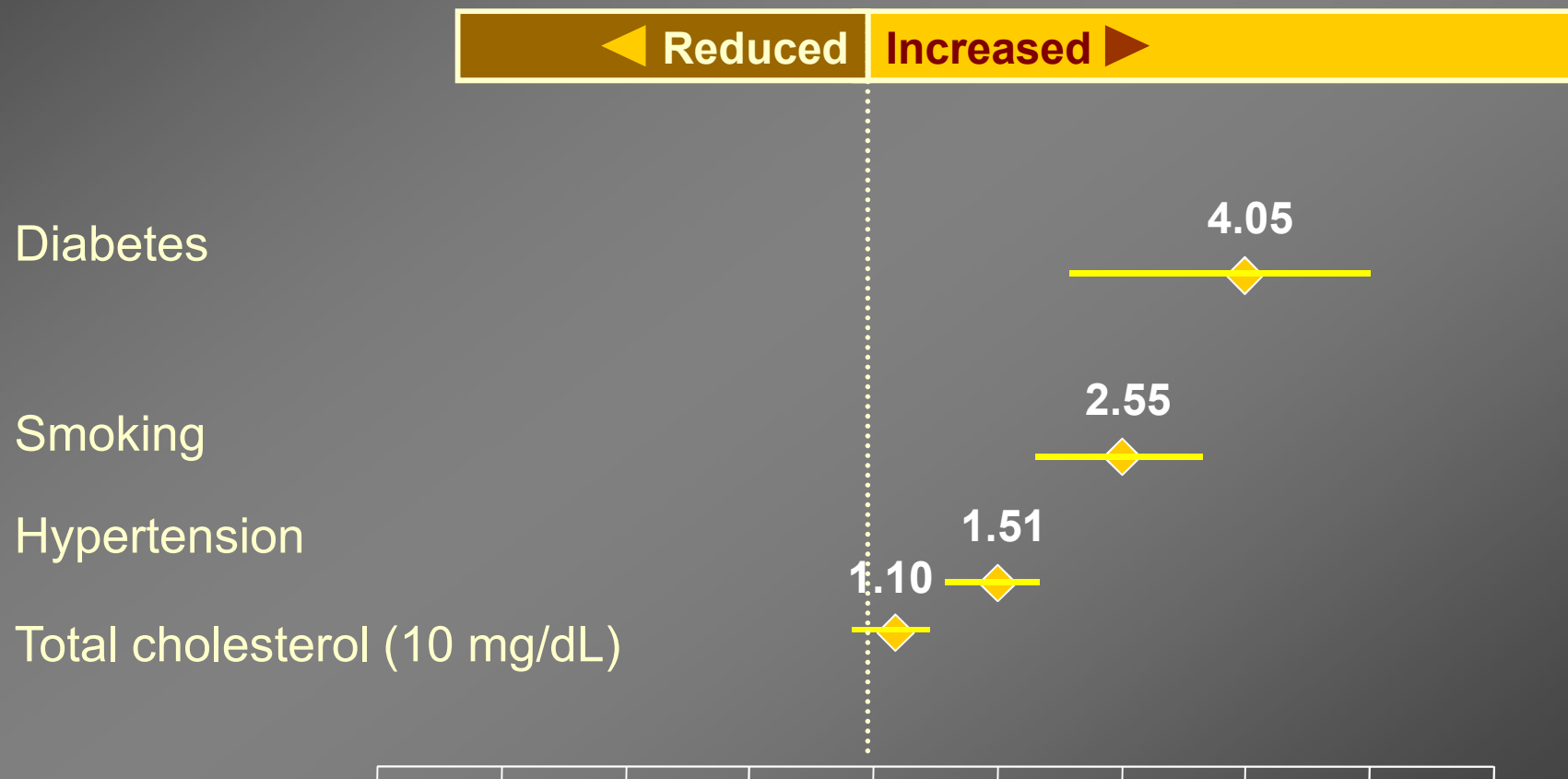
Adapted from Golomb BA, et al. In: Creager MA, ed. *Management of Peripheral Arterial Disease: Medical, Surgical and Interventional Aspects*; 2000:1-18.

Meijer WT, et al. *Arterioscler Thromb Vasc Biol.* 1998;18:185-192.

Criqui MH, et al. *Circulation.* 1985;71:510-515.

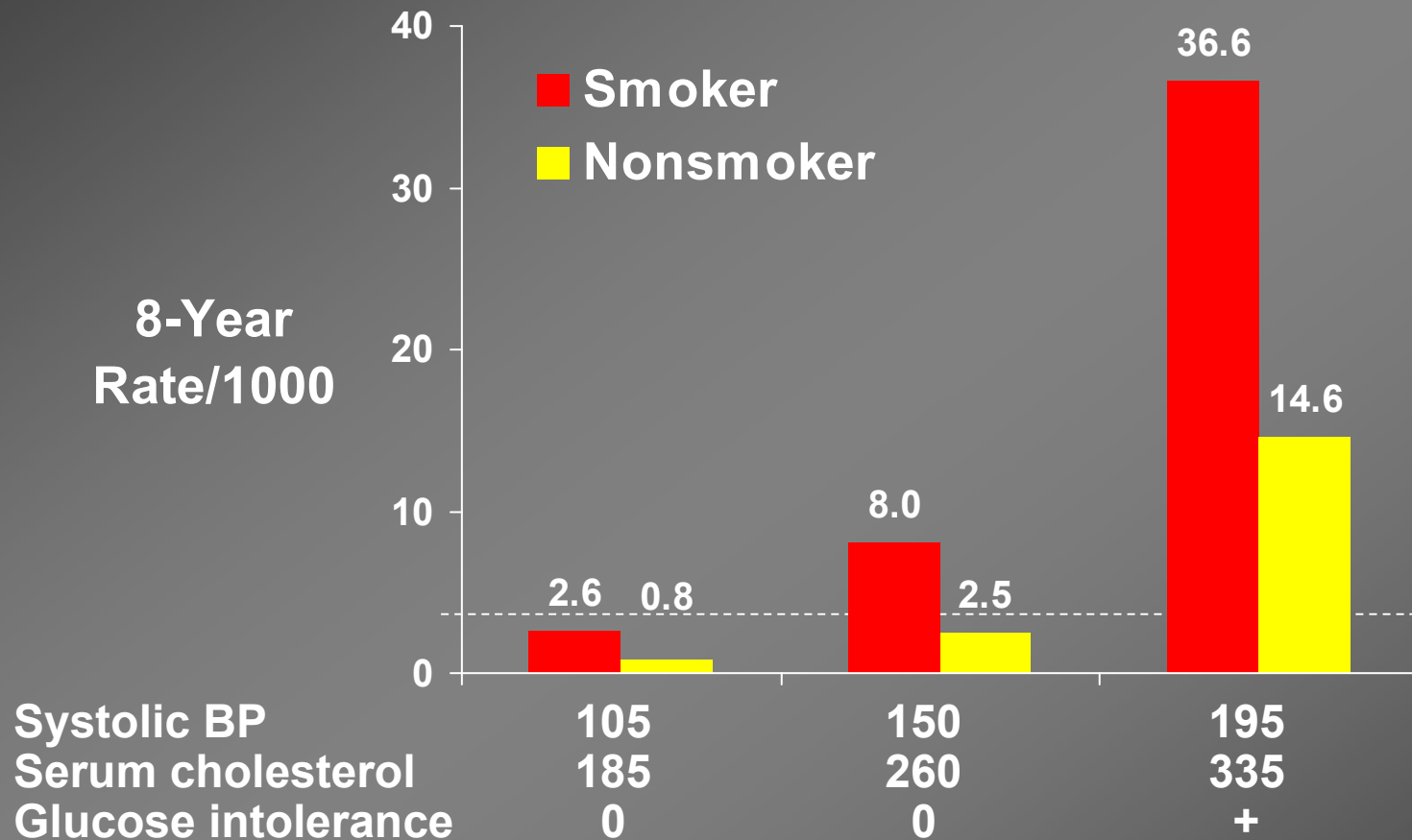
Independent Risk Factors for PAD*

Relative Risk vs the General Population



* PAD diagnosis based on ABI <0.90.

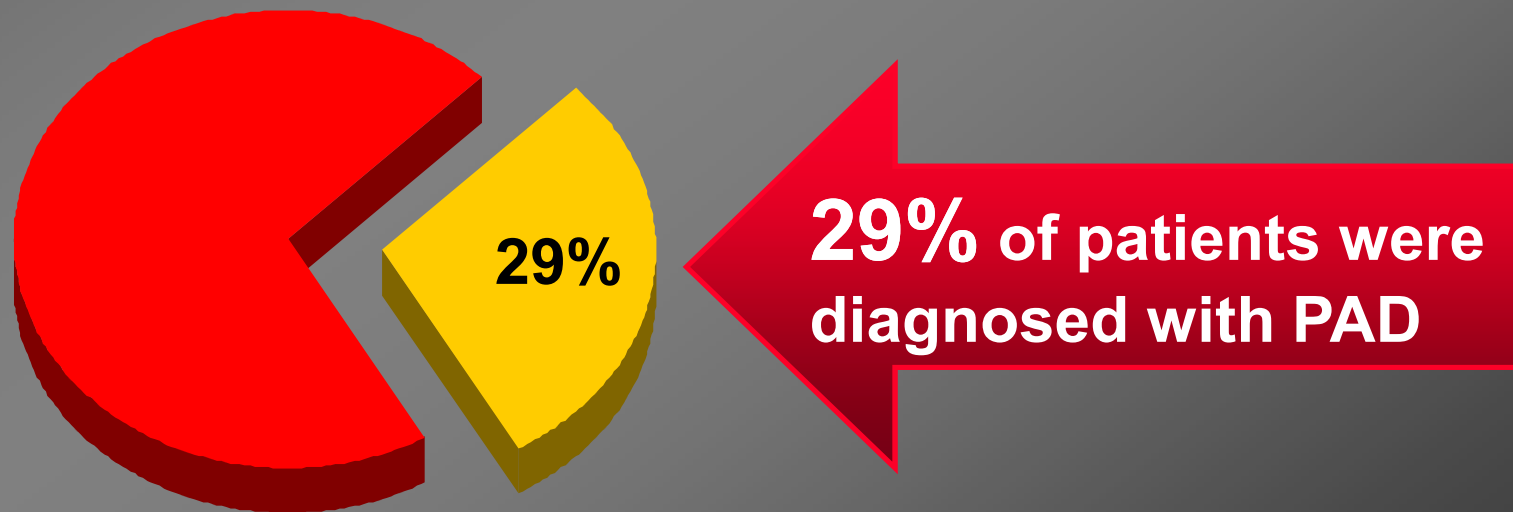
PAD Risk Factors are Synergistic



Adapted from TASC Working Group. *J Vasc Surg.* 2000;31(1 suppl):S1-S296.
Kannel WB et al. *J Am Geriatr Soc.* 1985;33:13-18.

Prevalence of PAD in At-Risk Patients

- The PARTNERS* program evaluated 6,979 patients in physicians' offices.
- Patient criteria:
 - ≥ 70 years, or
 - 50–69 years with a history of smoking and/or diabetes



* PARTNERS=PAD Awareness, Risk, and Treatment: New Resources for Survival.
Hirsch AT, et al. *JAMA*. 2001;286:1317-1324.

Typical vs Atypical Symptoms in Patients With Symptomatic PAD

Typical Symptoms¹

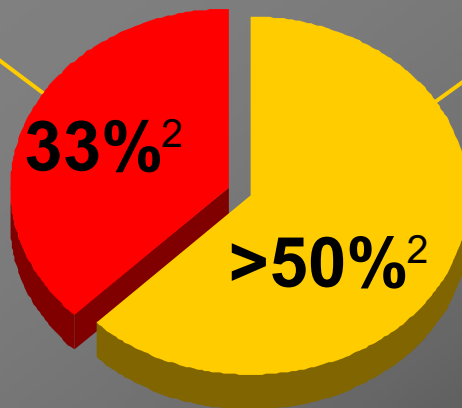
Intermittent claudication

- Exertional calf pain that
 - causes the patient to stop walking
 - resolves within 10 minutes of rest

Other nonspecific leg symptoms that may be indicative of PAD

Atypical Symptoms¹

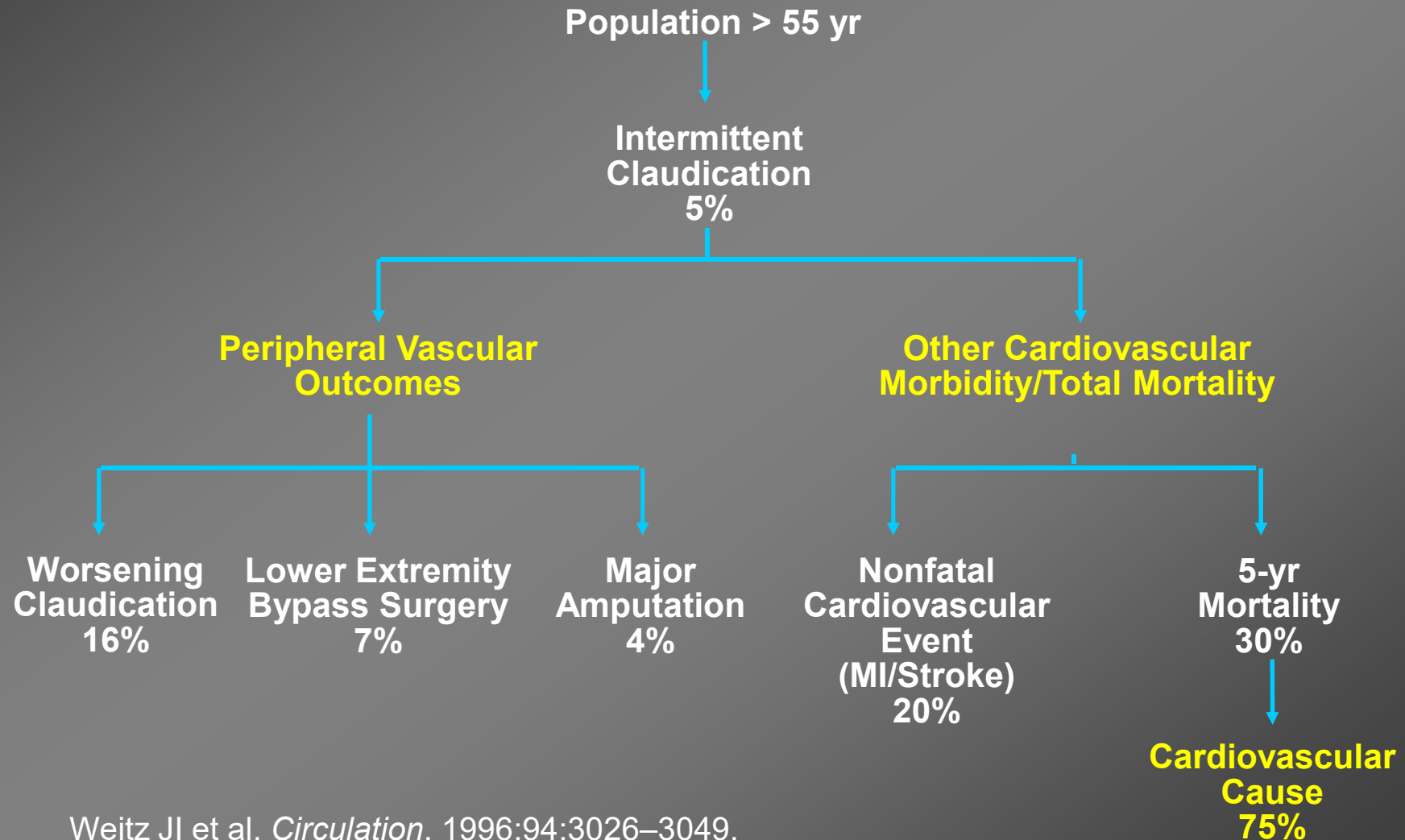
- Exertional leg pain that
 - may involve areas other than the calves
 - may not stop the patient from walking
 - may not resolve within 10 minutes of rest



1. McDermott MM et al. *JAMA*. 2001;286:1599-1606.

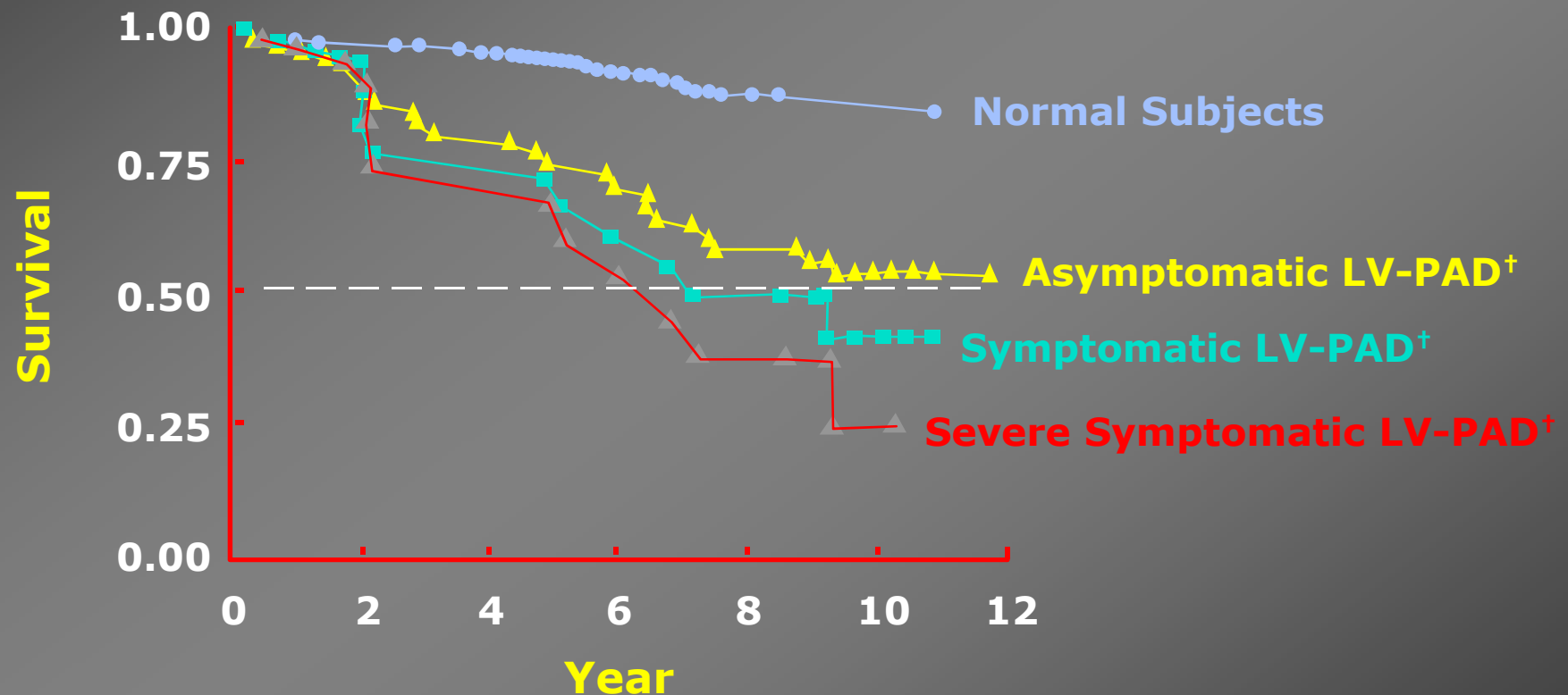
2. Hiatt WR. *N Engl J Med*. 2001;344:1608-1621.

Natural History Intermittent Claudication



Weitz JI et al. *Circulation*. 1996;94:3026–3049.

Impact of PAD on Mortality

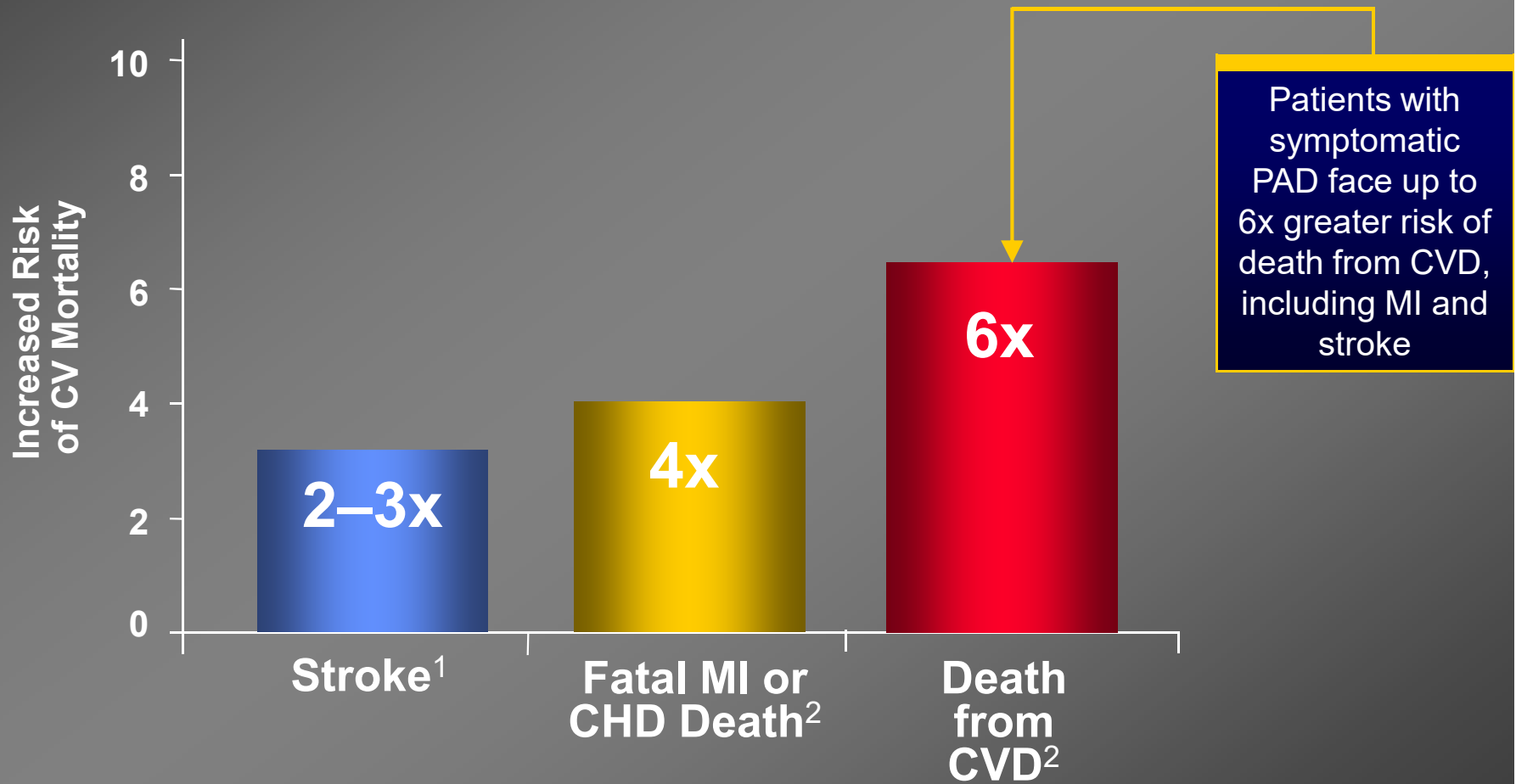


*Kaplan-Meier survival curves based on mortality from all causes.

[†]Large-vessel PAD.

Adapted from Criqui MH et al. *N Engl J Med.* 1992;326:381-386.

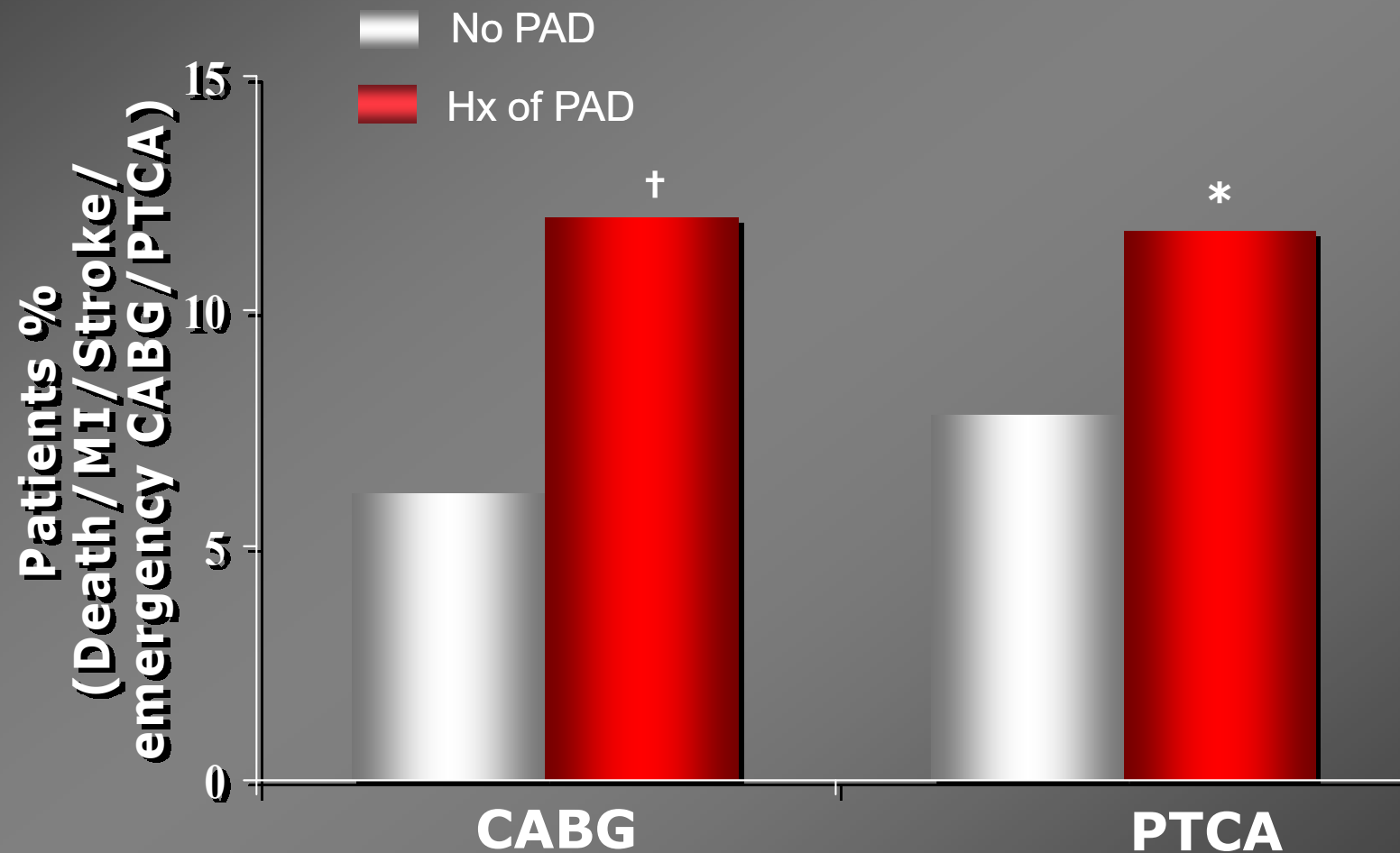
Cardiovascular Events with PAD



1. Kannel WB. *J Cardiovasc Risk*. 1994;1:333-339.

2. Criqui MH et al. *N Engl J Med*. 1992;326:381-386.

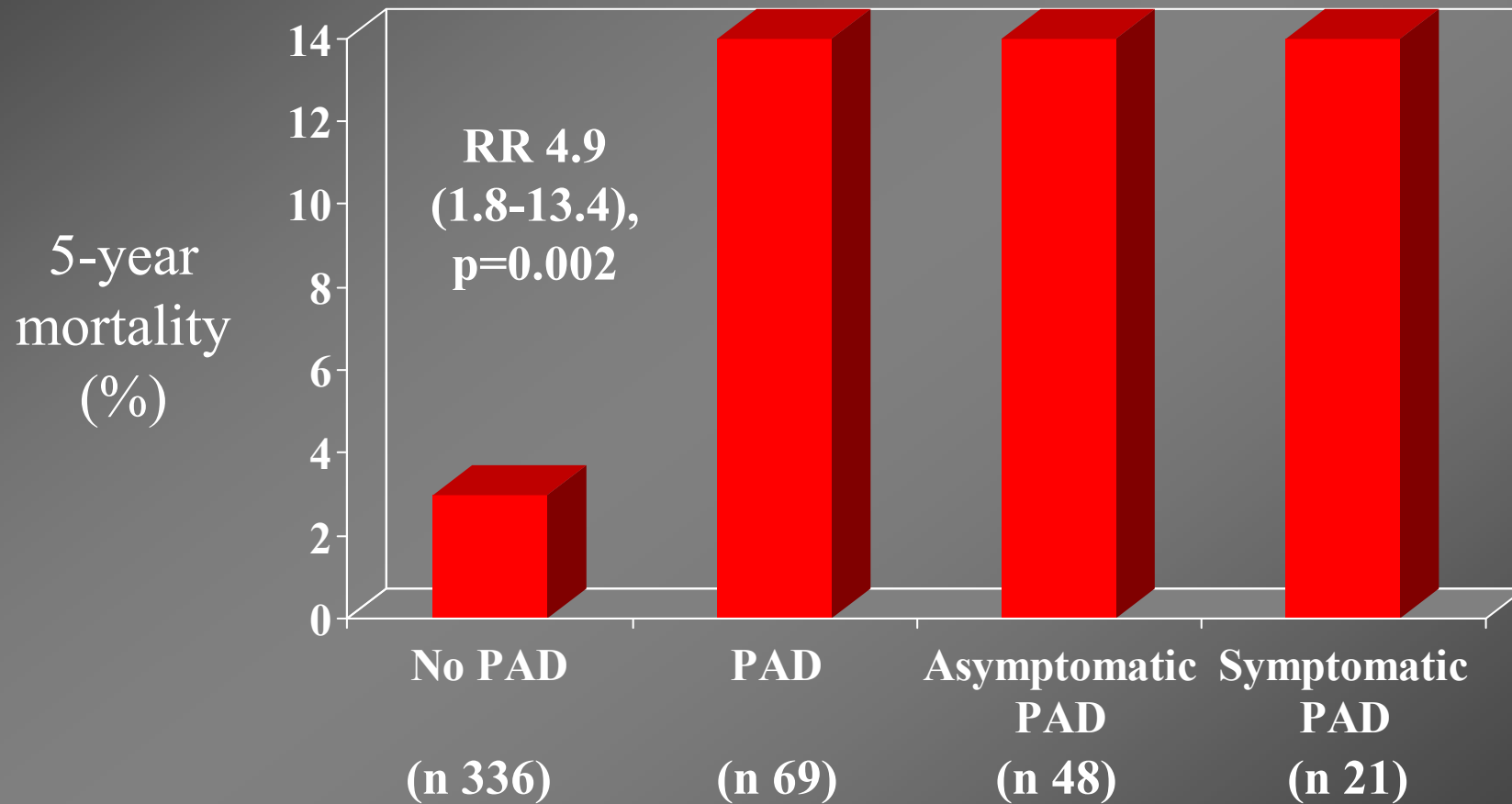
Increased Incidence of Periprocedural Complications in PAD



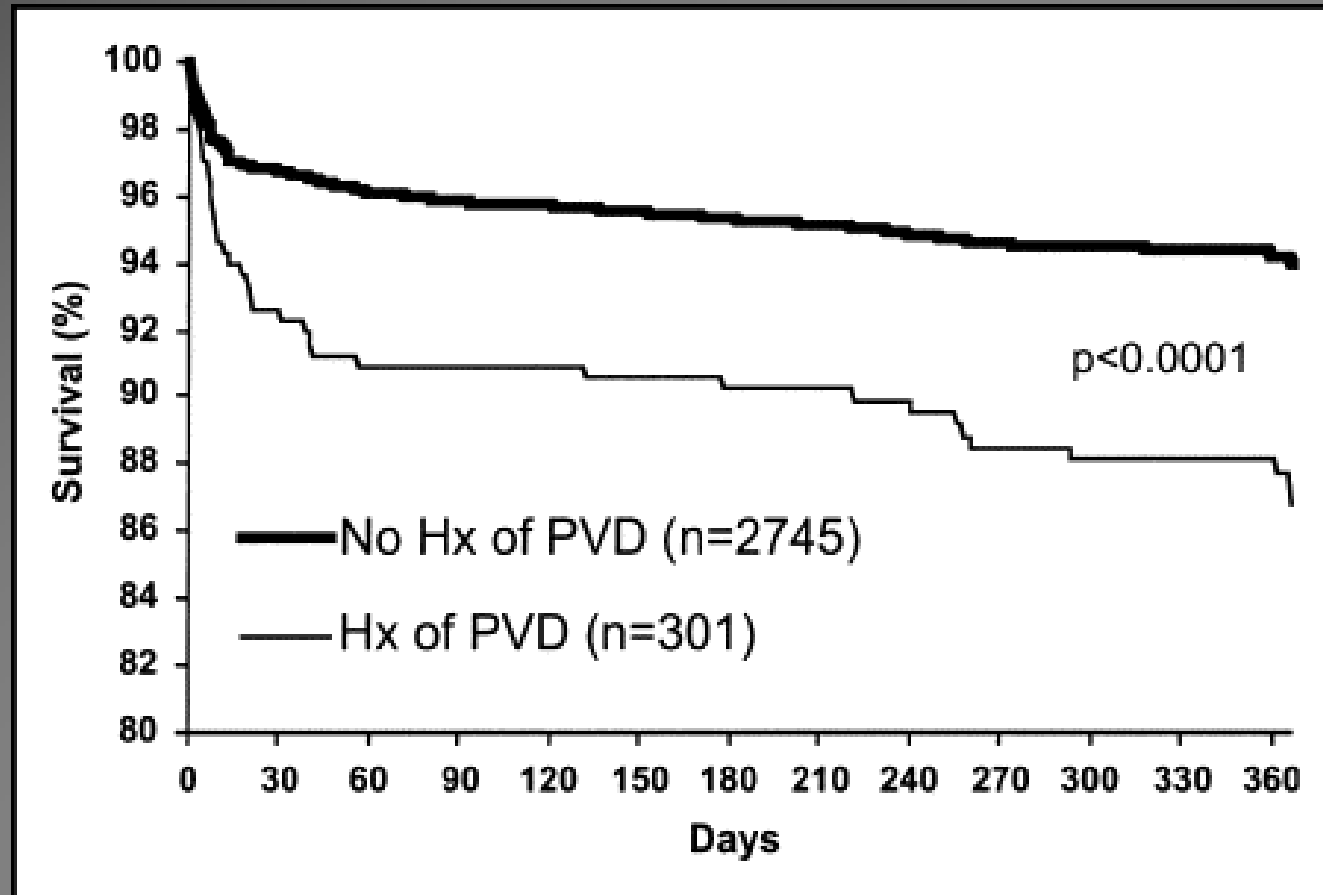
* $P < 0.05$, + $P < 0.01$. Note all comparisons are PAD vs. no PAD within treatment groups.

Rihal C et al. *Circulation* 1999; 100:171-177.

Prognostic importance of PAD in patients undergoing coronary revascularization



Effect of PVD on Mortality after AMI treated with PCI



Guerrero et al. Am J Cardiol 2005;96:649-654.

What factors may contribute to increase risk in PAD beyond CAD?

- Impaired endothelial function
- Heightened inflammation
- Propensity toward thrombosis
- Impaired functional capacity with reduced physical activity

What should we be thinking about in her treatment?

Treatment of PAD

Prevent Ischemic Events

Risk factor modification

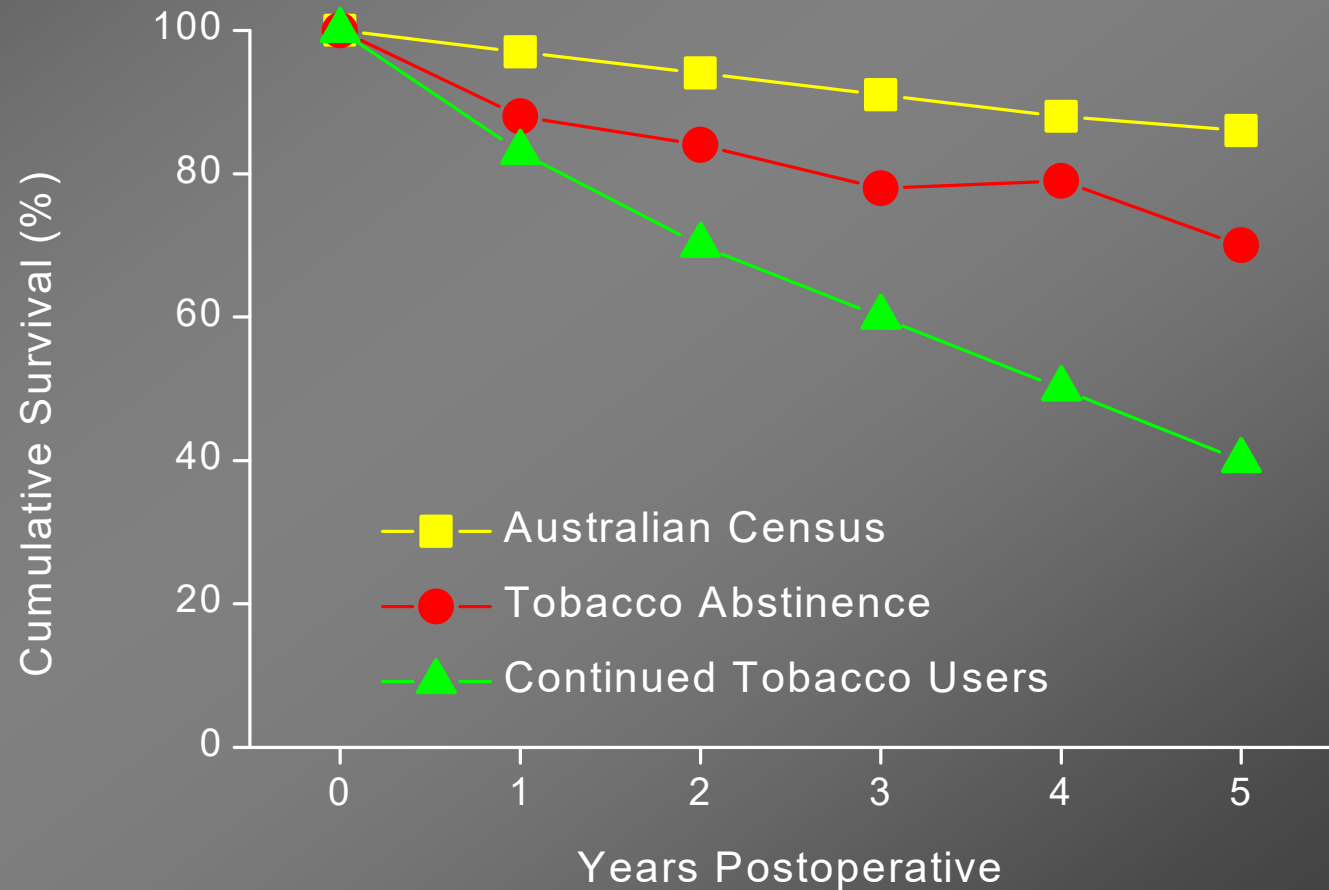
- **Smoking cessation**
 - Goal: complete cessation
- **Lipid management**
 - Target LDL < 100 mg/dL
- **Blood pressure control**
 - Goal <130/85 mm Hg
- **Blood sugar control**
 - Goal: HbA_{1c} <7%

Antiplatelet therapies

- **Aspirin or Clopidogrel**
 - Goal: reduction in risk of MI, stroke, and vascular death
 - Only clopidogrel is FDA approved
 - Many professional societies include ASA among first line agents in guidelines

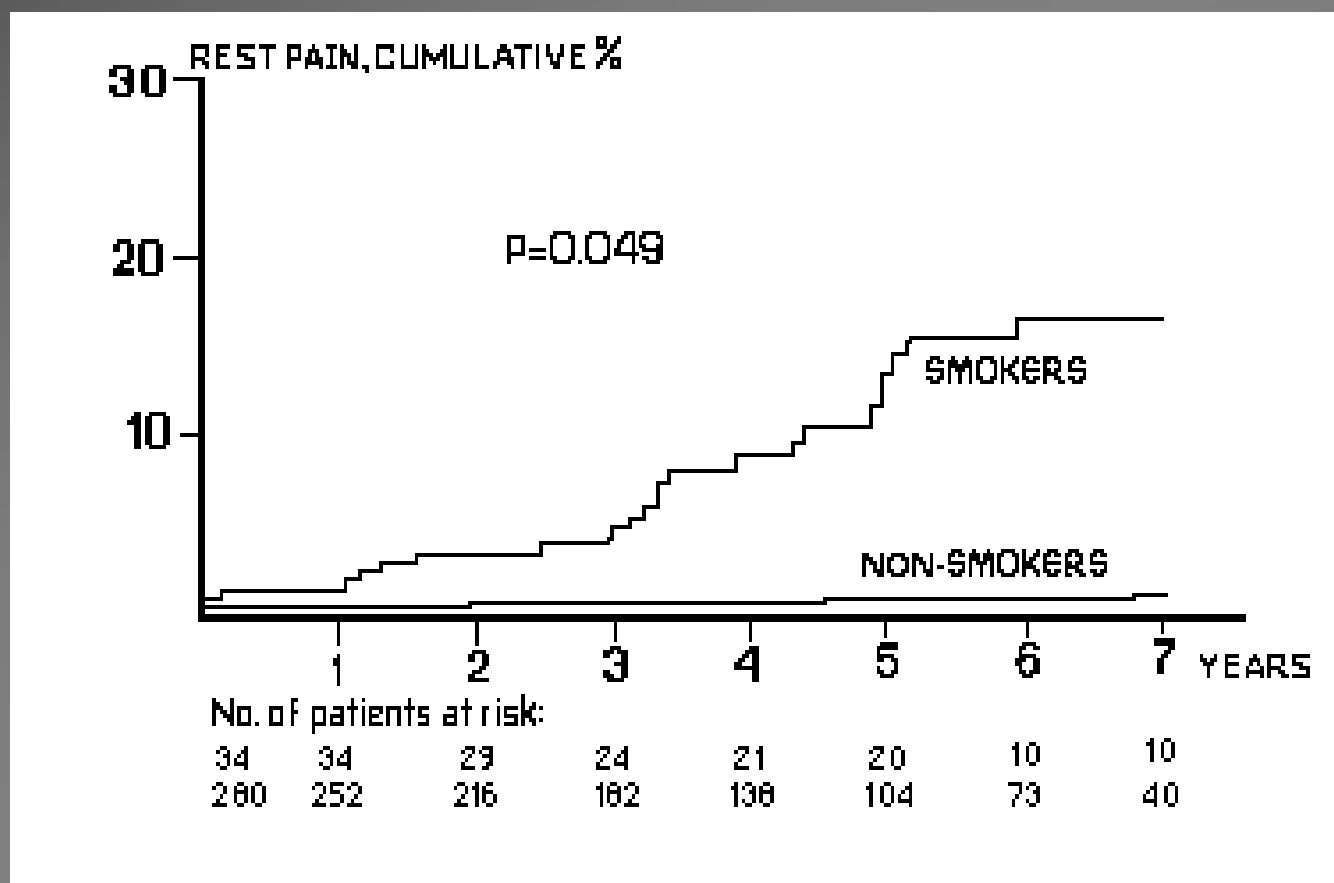
Effect of Smoking Cessation on Survival in PAD

131 Patients
Followed After
Bypass Graft or
Lumbar
Sympathectomy
Surgery



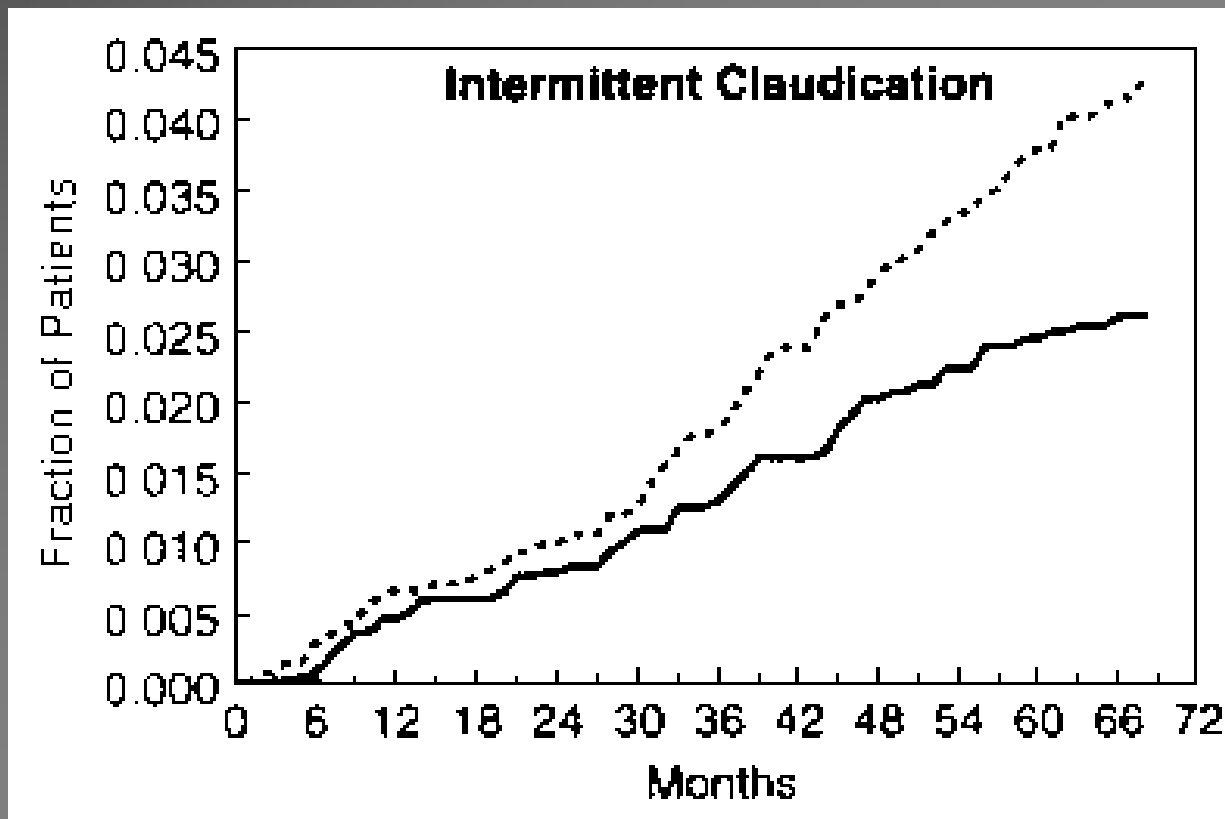
Faulkner et al. *Med J Aust* 1983;1:217.

Impact of Smoking Cessation on PAD



Jonason & Bergström. *Acta Med Scand* 1987;221:253-60

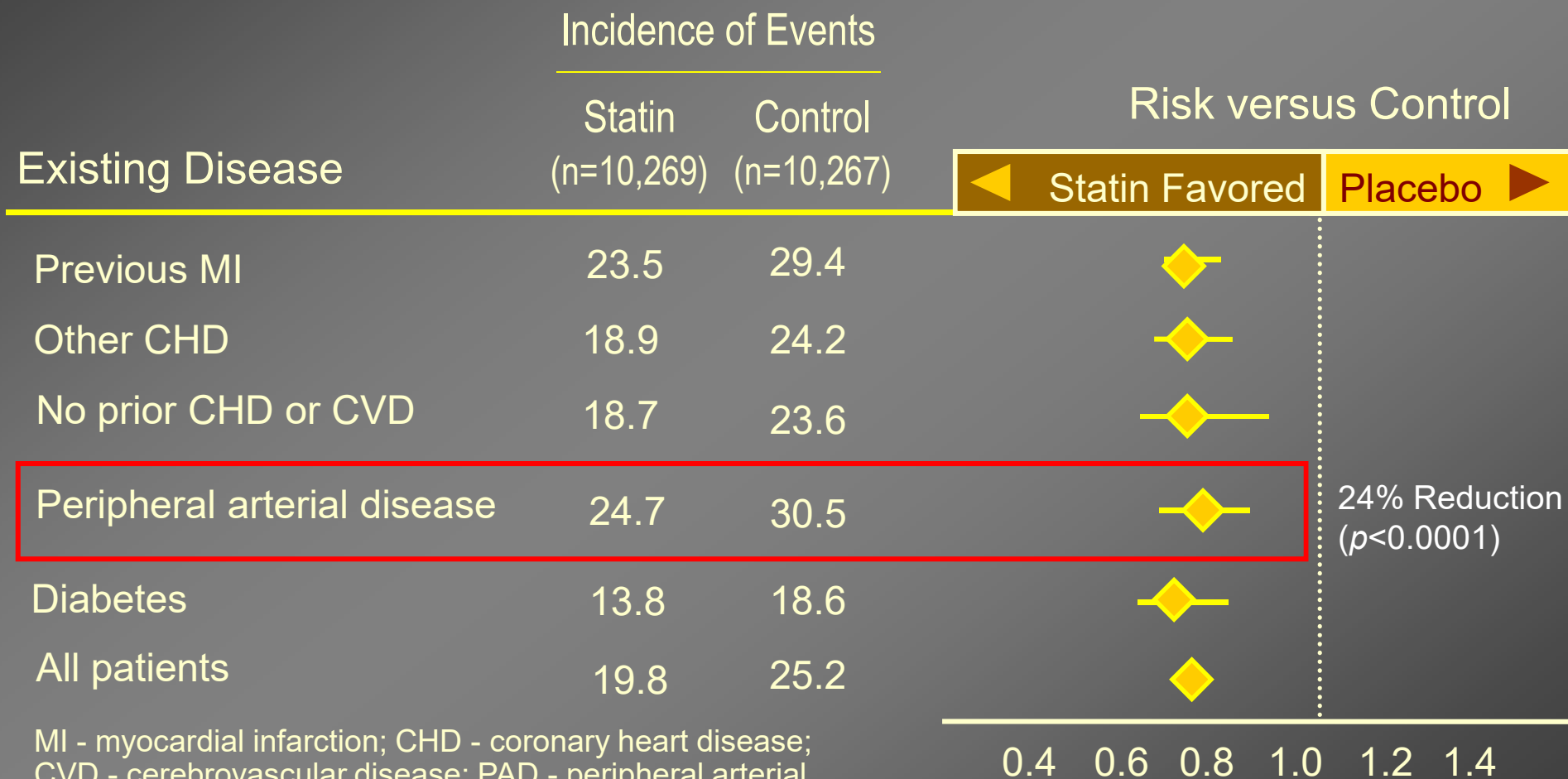
Cholesterol Reduction and the Development of Intermittent Claudication



Placebo
Simvastatin } 38%

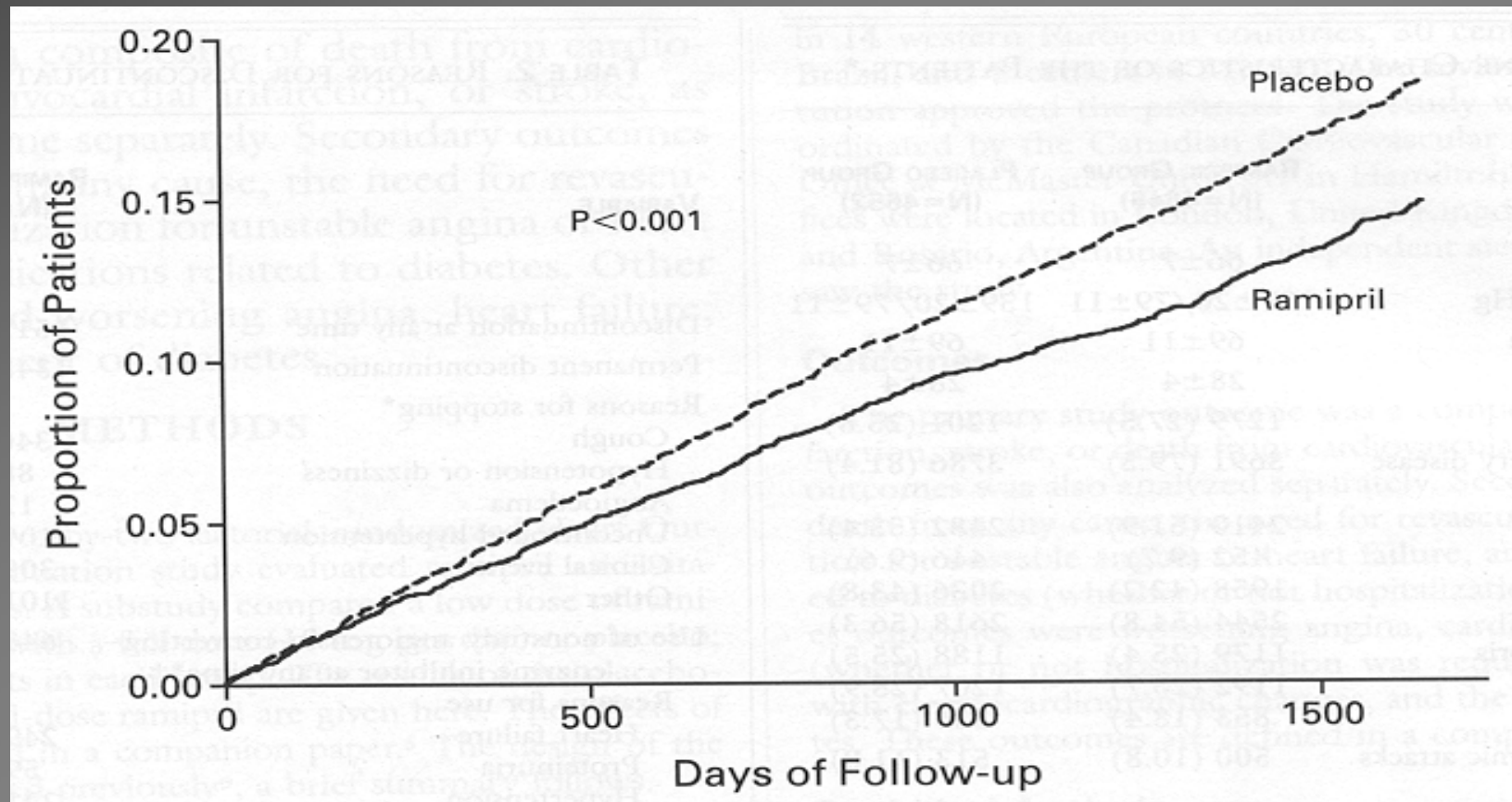
Scandinavian Simvastatin Survival Study
Pedersen et al. *Am J Card* 1998;81:333-5.

Heart Protection Study: Vascular Event by Prior Disease



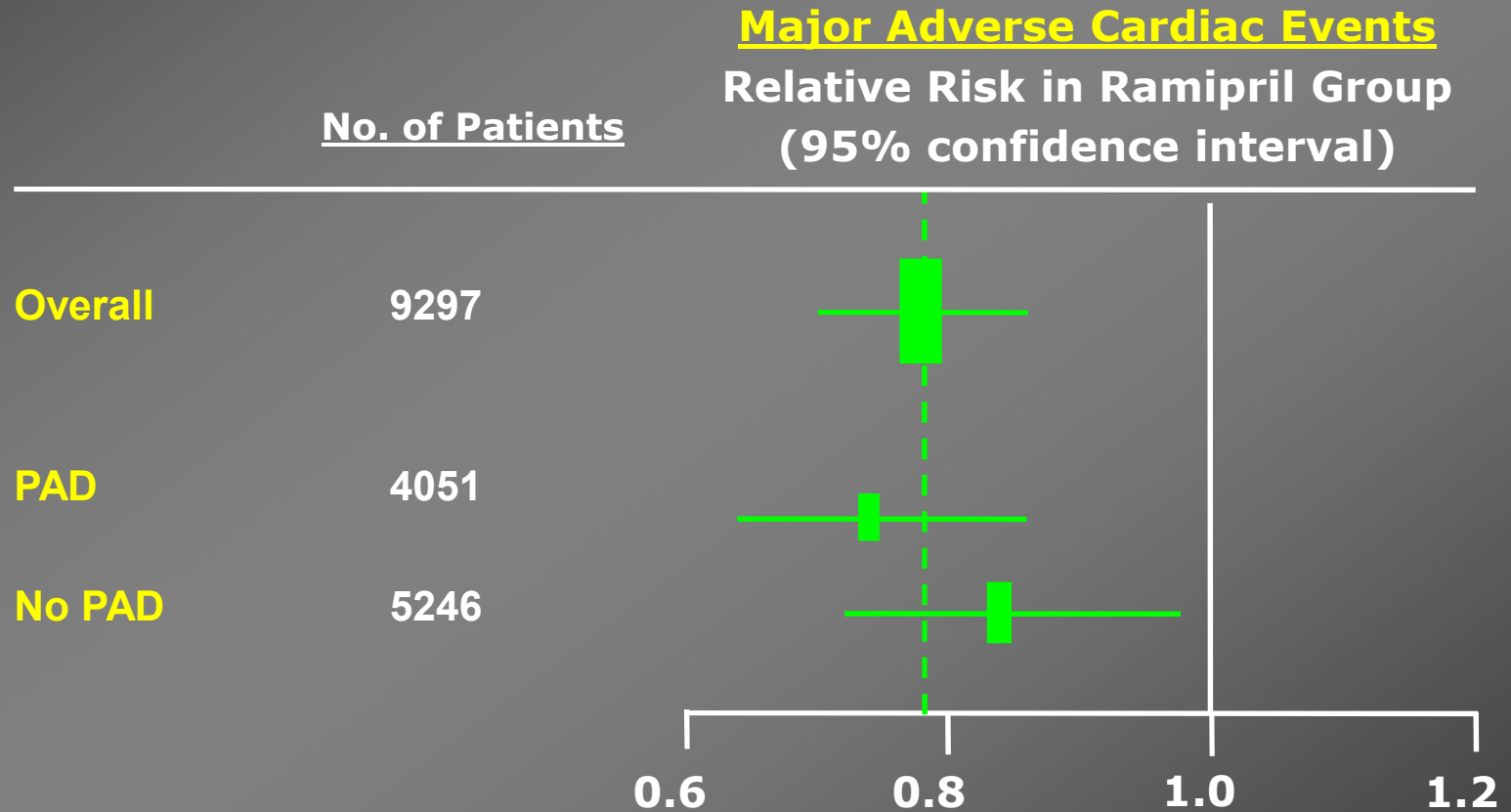
MI - myocardial infarction; CHD - coronary heart disease;
CVD - cerebrovascular disease; PAD - peripheral arterial
disease; CI - confidence interval; SE - standard error

ACE Inhibition and Cardiovascular Events in High-Risk Patients



The Heart Outcome Prevention Evaluation Study.
NEJM 2000;342:145-53.

Effect of ACE Inhibition on Cardiovascular Events in PAD



The Heart Outcome Prevention Evaluation Study. *NEJM* 2000;342:145-53.

ACC/AHA 2005 Guidelines

Risk Factor Management in PAD

Lipid-lowering
drugs



All patients with PAD: Statin treatment to achieve LDL level <100 mg/dL



Patients with very high risk of ischemic events: Consider LDL of <70 mg/dL

Antihypertensive
drugs



Target blood pressure $<140/90$ mm Hg to reduce cardiovascular risk



If comorbid diabetes or chronic renal disease, target blood pressure $<130/80$ mm Hg

Recommendations for Smoking Cessation



NEW

Patients who are smokers or former smokers should be asked about status of tobacco use at every visit.



NEW

Patients should be assisted with counseling and developing a plan for quitting that may include pharmacotherapy and/or referral to a smoking cessation program.



MODIFIED

Individuals with lower extremity PAD who smoke cigarettes or use other forms of tobacco should be advised by each of their clinicians to stop smoking and offered behavioral and pharmacological treatment.



NEW

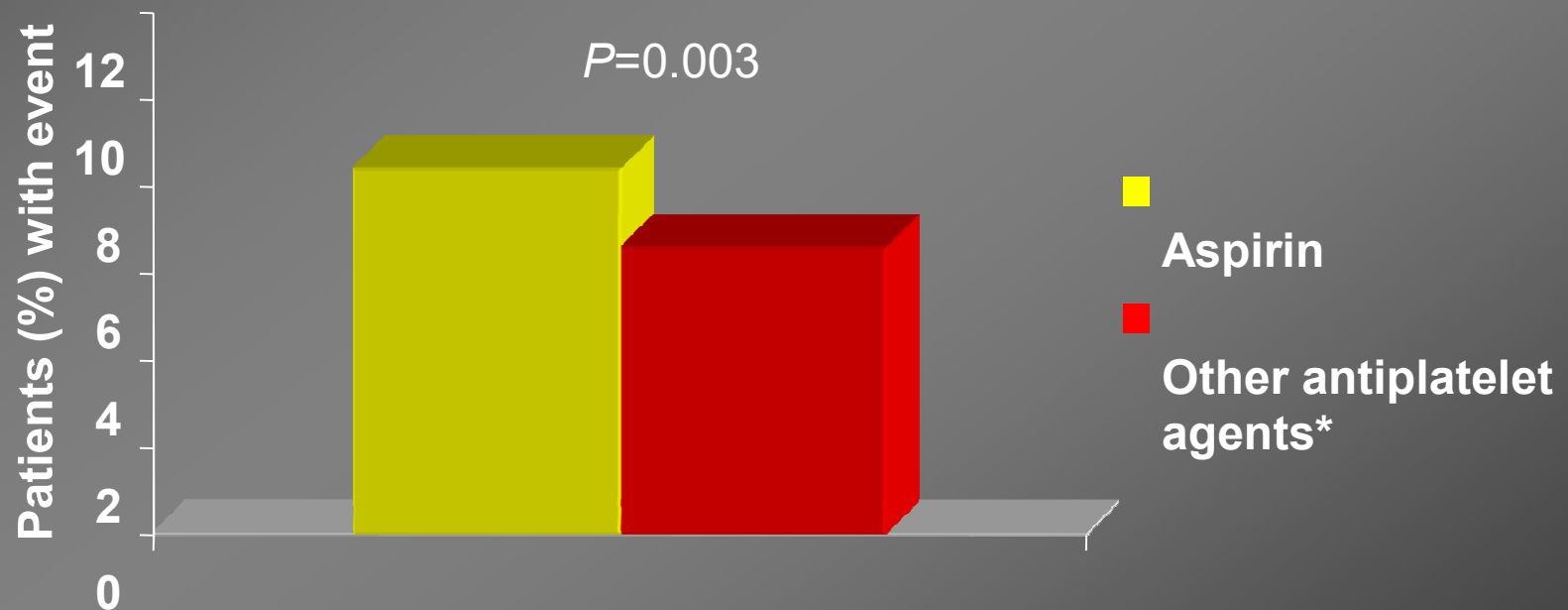
In the absence of contraindication or other compelling clinical indication, 1 or more of the following pharmacological therapies should be offered: varenicline, bupropion, and nicotine replacement therapy.

Effect of Antiplatelet Therapy on Cardiovascular Events in PAD

- 42 clinical trials
- 9,214 patients with PAD
- 23% reduction in serious adverse vascular events ($P=0.004$)
- Benefits similar among PAD subtypes (intermittent claudication, peripheral grafting, and peripheral angioplasty)

Effect of Aspirin vs Other Antiplatelet Agents in Reducing Vascular Events in Patients with PAD*

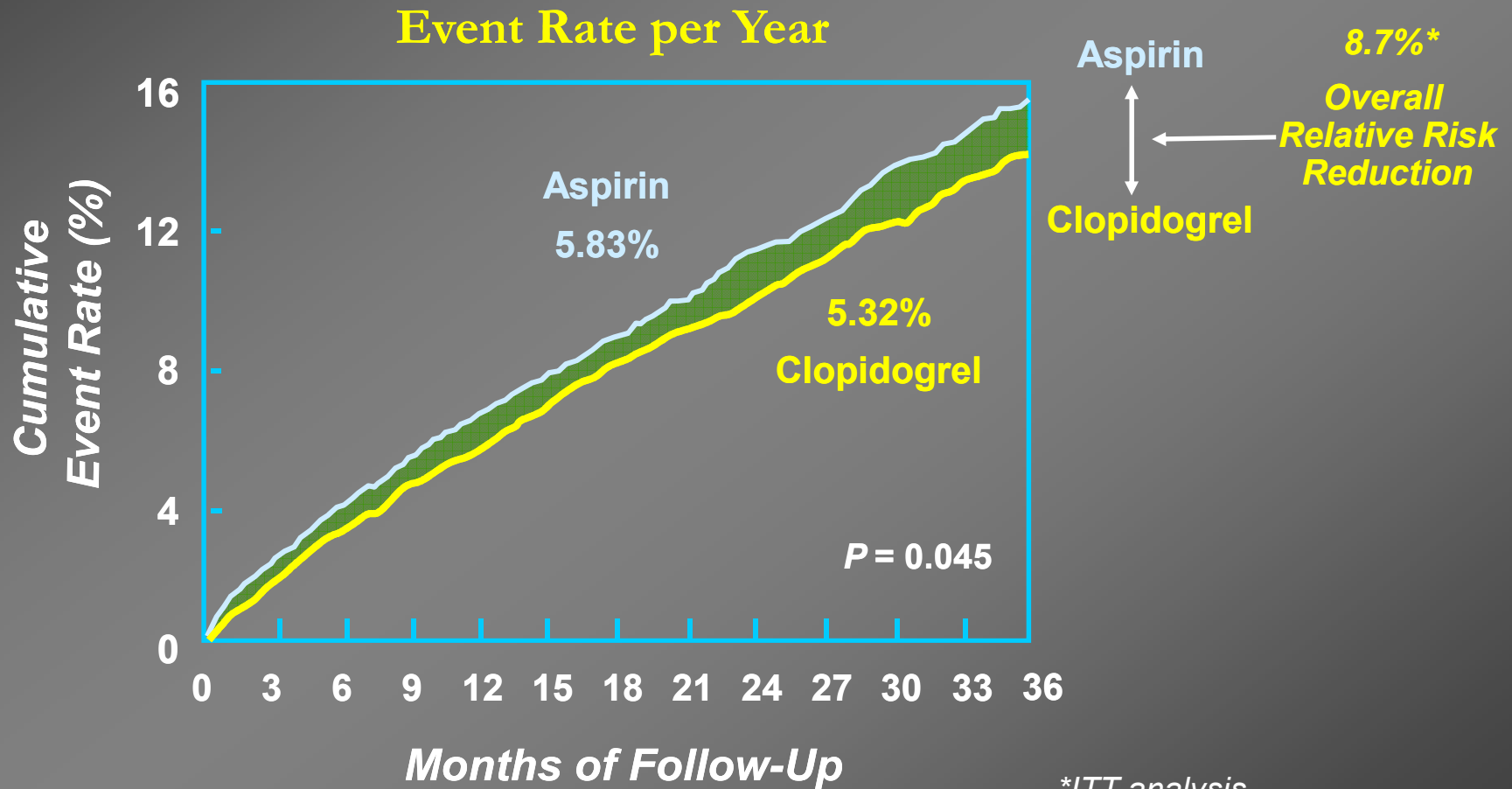
Treatment with other antiplatelet therapy resulted in a 24% reduction in vascular events compared with aspirin alone



*Meta-analysis. Other antiplatelet agents included ticlopidine, clopidogrel, or dipyridamole/aspirin combination.

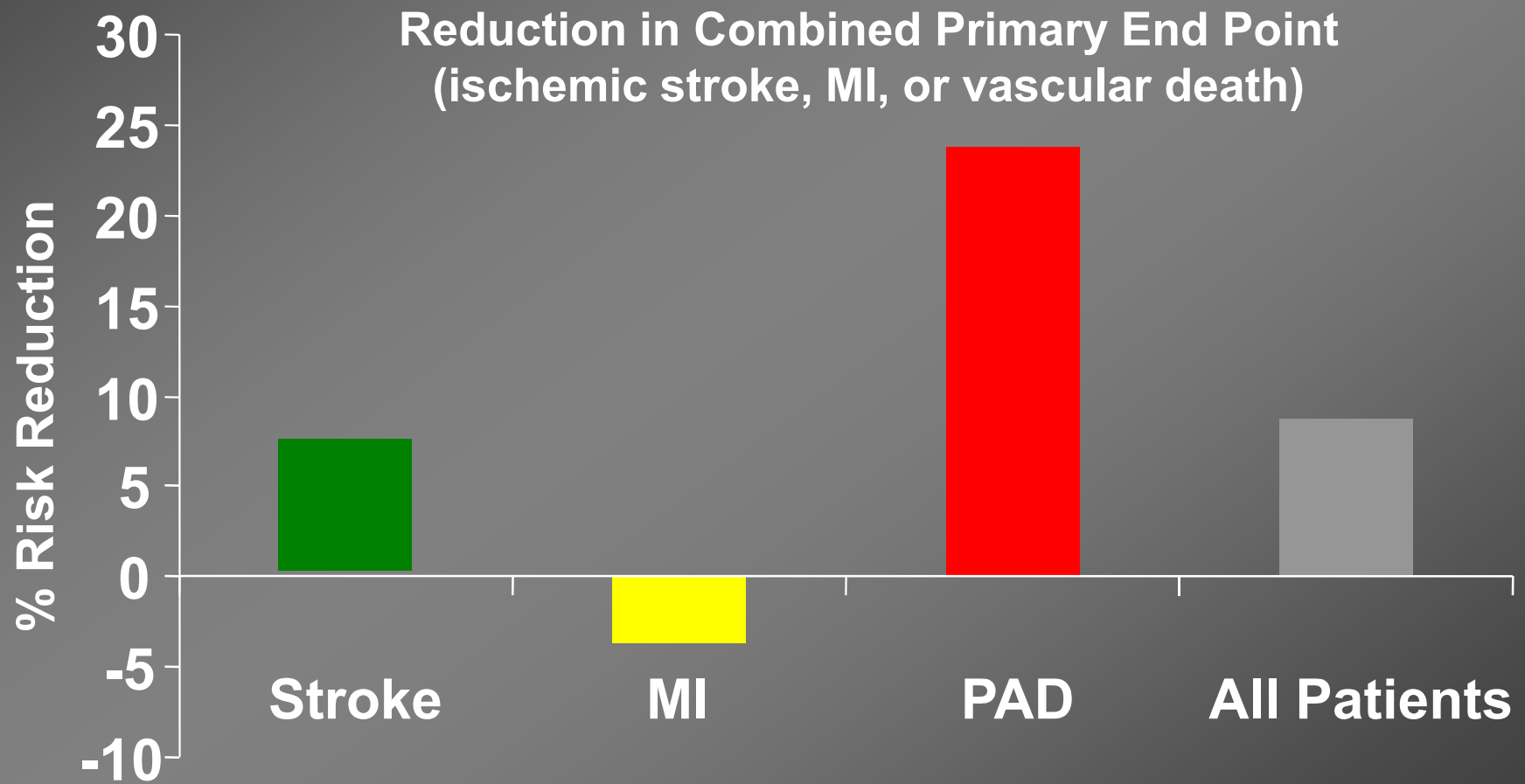
Derived from Robless P et al. *Br J Surg.* 2001;88:787-800.

Clopidogrel vs. Aspirin in Prevention of Ischemic Events



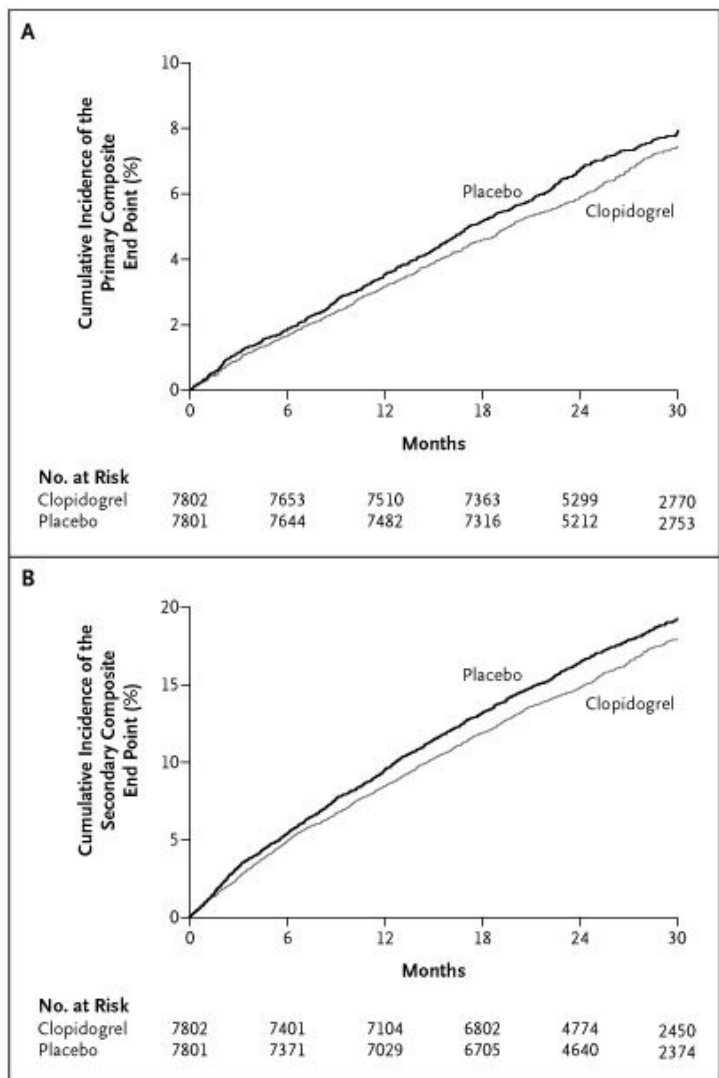
*ITT analysis.
CAPRIE Steering Committee.
Lancet 1996;348:1329-1339.

Risk Reduction of Clopidogrel vs. Aspirin



CAPRIE Steering Committee. *Lancet*. 1996;348:1329-1339.

Effect of Dual Antiplatelet Therapy with High Risk Atherosclerotic Disease



Safety and Efficacy of Dual Antiplatelet Therapy with High Risk Atherosclerotic Disease

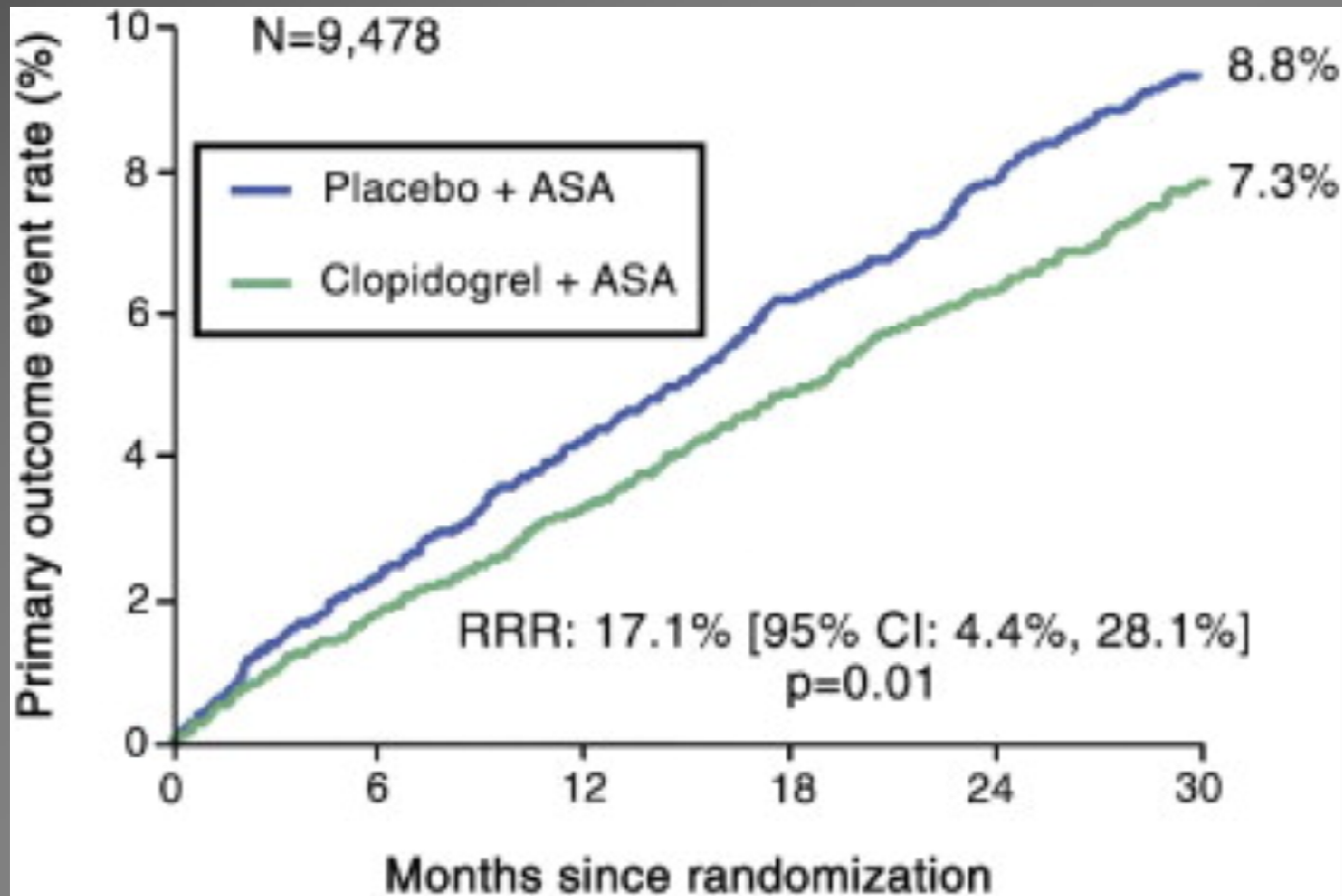
Table 4. Composite and Individual Primary and Secondary End Points.

End Point	Clopidogrel plus Aspirin (N=7802)	Placebo plus Aspirin (N=7801)	Relative Risk (95% CI)*	P Value
	no. (%)			
Efficacy end points				
Primary efficacy end point	534 (6.8)	573 (7.3)	0.93 (0.83–1.05)	0.22
Death from any cause	371 (4.8)	374 (4.8)	0.99 (0.86–1.14)	0.90
Death from cardiovascular causes	238 (3.1)	229 (2.9)	1.04 (0.87–1.25)	0.68
Myocardial infarction (nonfatal)	146 (1.9)	155 (2.0)	0.94 (0.75–1.18)	0.59
Ischemic stroke (nonfatal)	132 (1.7)	163 (2.1)	0.81 (0.64–1.02)	0.07
Stroke (nonfatal)	150 (1.9)	189 (2.4)	0.79 (0.64–0.98)	0.03
Secondary efficacy end point†	1301 (16.7)	1395 (17.9)	0.92 (0.86–0.995)	0.04
Hospitalization for unstable angina, transient ischemic attack, or revascularization	866 (11.1)	957 (12.3)	0.90 (0.82–0.98)	0.02
Safety end points				
Severe bleeding	130 (1.7)	104 (1.3)	1.25 (0.97–1.61)	0.09
Fatal bleeding	26 (0.3)	17 (0.2)	1.53 (0.83–2.82)	0.17
Primary intracranial hemorrhage	26 (0.3)	27 (0.3)	0.96 (0.56–1.65)	0.89
Moderate bleeding	164 (2.1)	101 (1.3)	1.62 (1.27–2.08)	<0.001

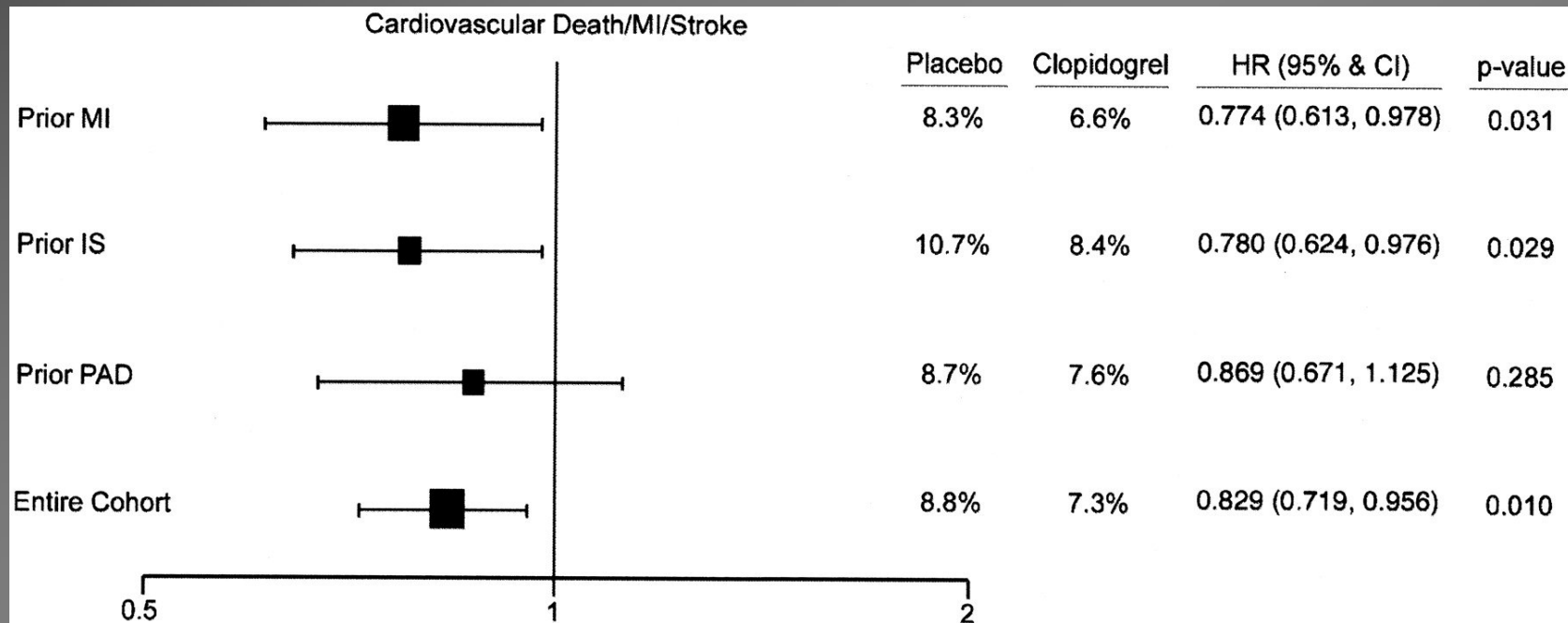
* CI denotes confidence interval.

† The secondary efficacy end point was the first occurrence of myocardial infarction, stroke, death from cardiovascular causes, or hospitalization for unstable angina, a transient ischemic attack, or a revascularization procedure (coronary, cerebral, or peripheral).

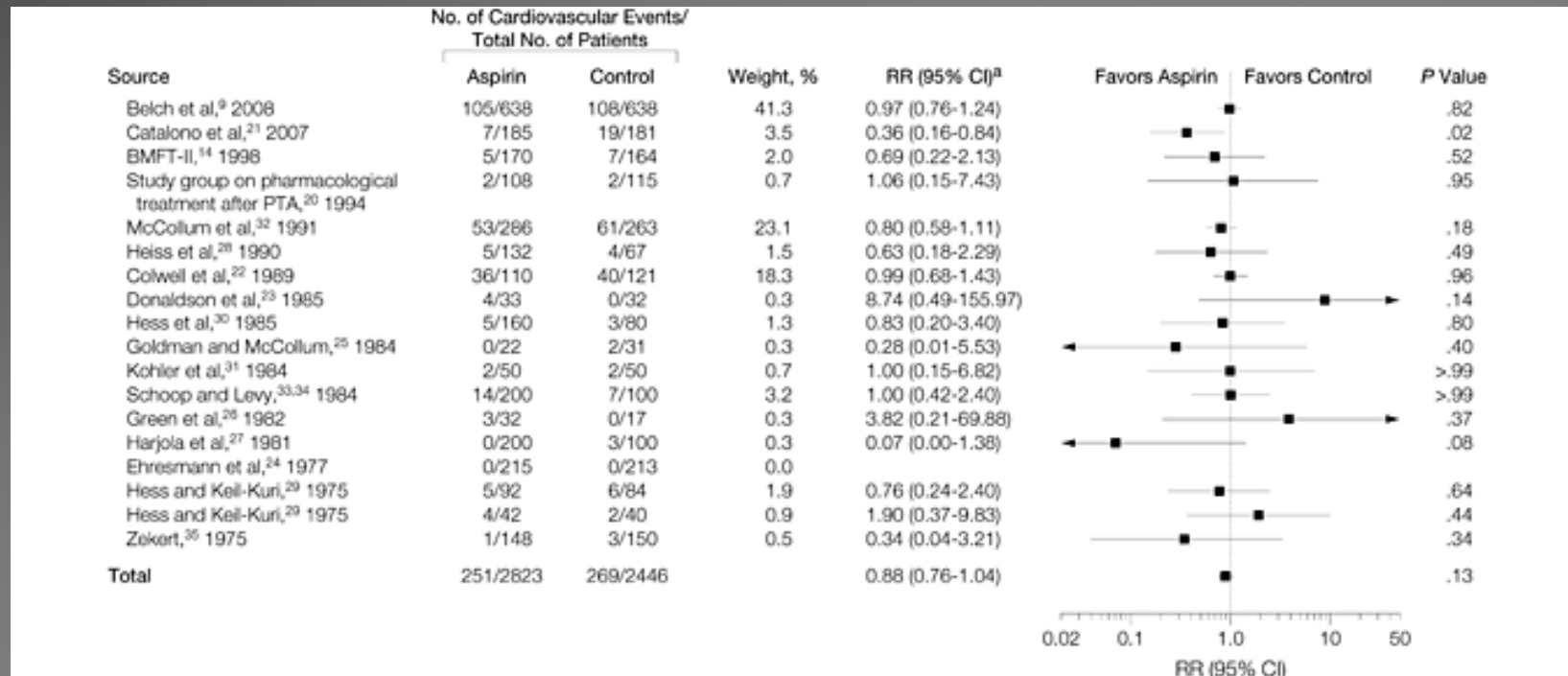
Effect of Dual Antiplatelet Therapy with Established Atherosclerotic Disease



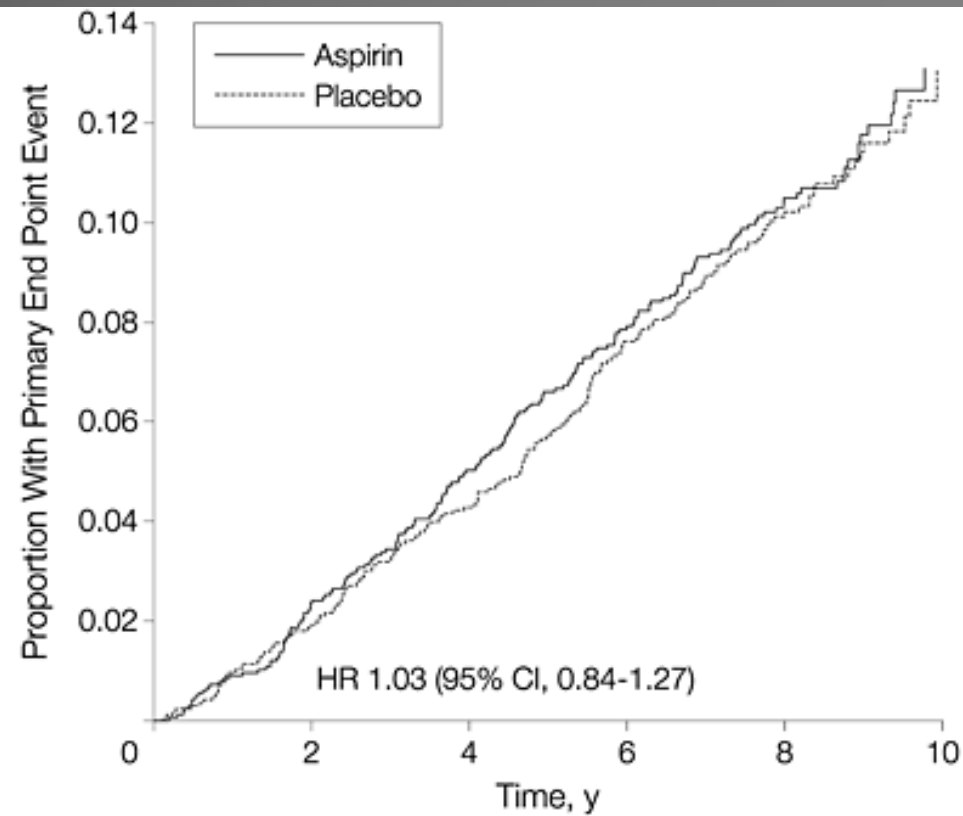
Effect of Dual Antiplatelet Therapy with Established Atherosclerotic Disease



Effect of Aspirin on the Prevention of Cardiovascular Events in PAD

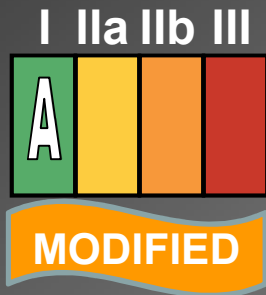


Aspirin for Prevention Cardiovascular Events with Low ABI

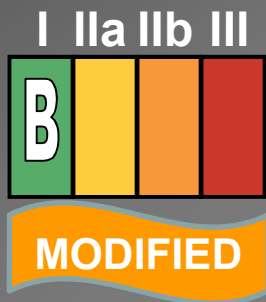


No. at risk						
Aspirin	1675	1618	1555	1473	946	124
Placebo	1675	1634	1566	1474	935	119

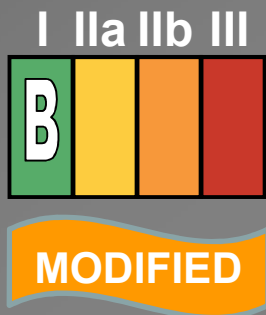
Recommendations for Antiplatelet and Antithrombotic Drugs



Antiplatelet therapy is indicated to reduce the risk of MI, stroke, and vascular death in symptomatic PAD



Aspirin, 75 to 325 mg, is recommended as safe and effective antiplatelet therapy.



Clopidogrel (75 mg per day) is recommended as a safe and effective alternative antiplatelet therapy to aspirin

Recommendations for Antiplatelet and Antithrombotic Drugs



Antiplatelet therapy can be useful to reduce the risk of MI, stroke, or vascular death in asymptomatic individuals with an ABI ≤ 0.90 .

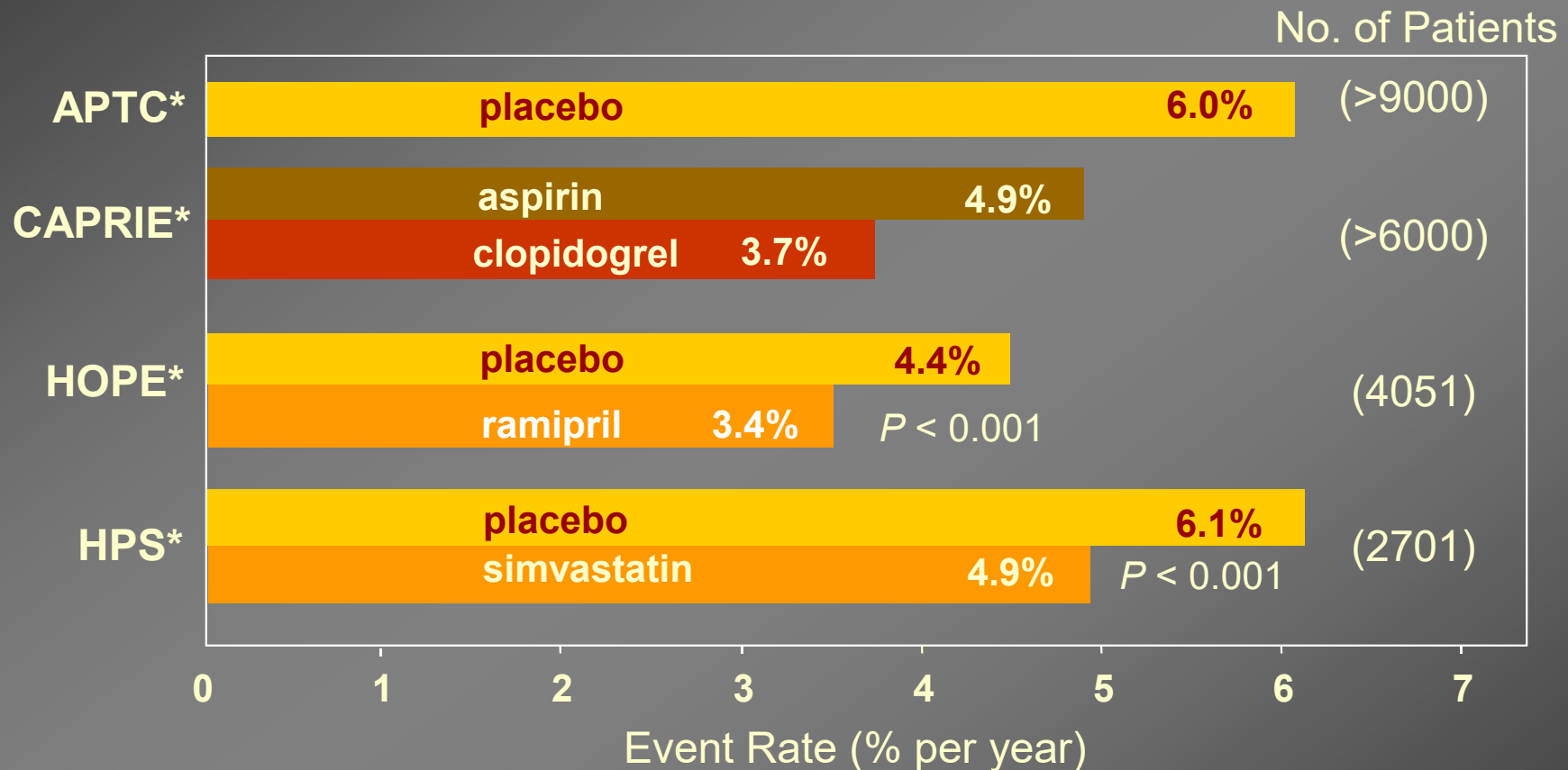


The usefulness of antiplatelet therapy to reduce the risk of MI, stroke, or vascular death in asymptomatic individuals with borderline abnormal ABI, defined as 0.91 to 0.99, is not well established.



The combination of aspirin and clopidogrel may be considered to reduce the risk of cardiovascular events in symptomatic PAD, not at increased risk of bleeding and at high perceived cardiovascular risk

Risk Reduction with ACE-inhibitors, Statins, and Antiplatelet Therapy in PAD



*PAD subgroups only.

APTC Antiplatelet Trialists' Collaboration. *BMJ*. 1994;308:81-106.

CAPRIE Steering Committee. *Lancet*. 1996;348:1329-1339.

HOPE Study Investigators. *N Engl J Med*. 2000;342:145-153.

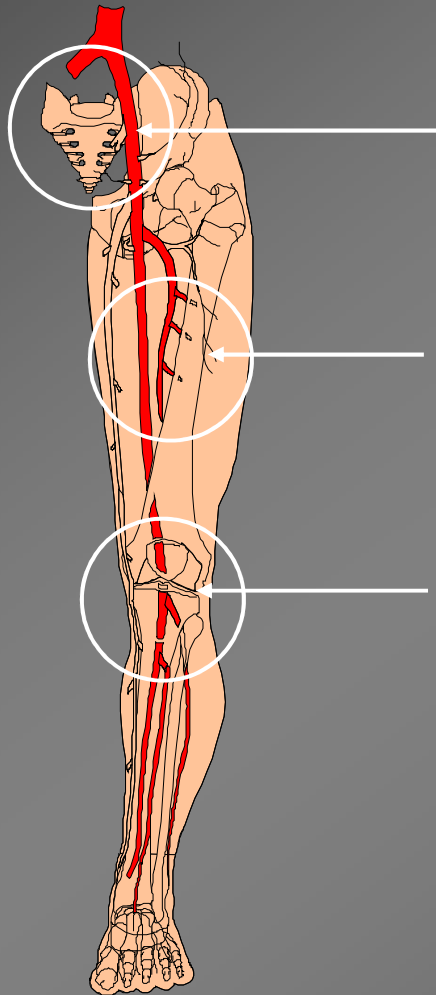
Heart Protection Study Collaborative Group. *Lancet*. 2002;360:7-22.

PAD Case #2

- A 58 year old male presents with exertional left calf discomfort at ½ block
- Symptoms occur reproducibly with exertion and relieved by rest
- He has a history of DM, HTN, tobacco use, and known PAD with prior left femoral-popliteal bypass surgery
- Medications include lisinopril, metoprolol, atorvastatin, aspirin 81mg, and metformin.
- Exam reveals palpable femoral pulses without bruits, diminished popliteal and distal pulse on left, and no positional color changes or skin breakdown

How do we establish a diagnosis of PAD
or assess severity and localize disease?

Common Sites of Claudication



Obstruction in
Aorta or
iliac artery



Ischemia in
Buttock, hip,
thigh

Femoral artery
or branches



Thigh,
calf

Popliteal artery
or distal



Calf, ankle,
foot

Effect of Claudication on Peak Oxygen Consumption

	Normal	IC
Peak $\dot{V}O_2$	30–40 mL/kg/min	15–20 mL/kg/min*

*Approximates peak oxygen uptake of patients with **NYHA class III CHF.**

Hiatt WR. *J Appl Physiol.* 1992;73:346-53.
Hiatt WR. *Circulation.* 1990;81:602-9.

Does the Patient Have Intermittent Claudication?

	Claudication	Pseudoclaudication
Characteristic of discomfort	Cramping, tightness, aching, fatigue	Same, tingling, burning, numbness
Location of discomfort	Buttock, hip, thigh, calf, foot	Same
Exercise-induced	Yes	Variable
Distance	Consistent	Variable
Occurs with standing	No	Yes
Action for relief	Stand	Sit, change position
Time to relief	Less than 5 minutes	Up to 30 minutes

Diagnostic Testing

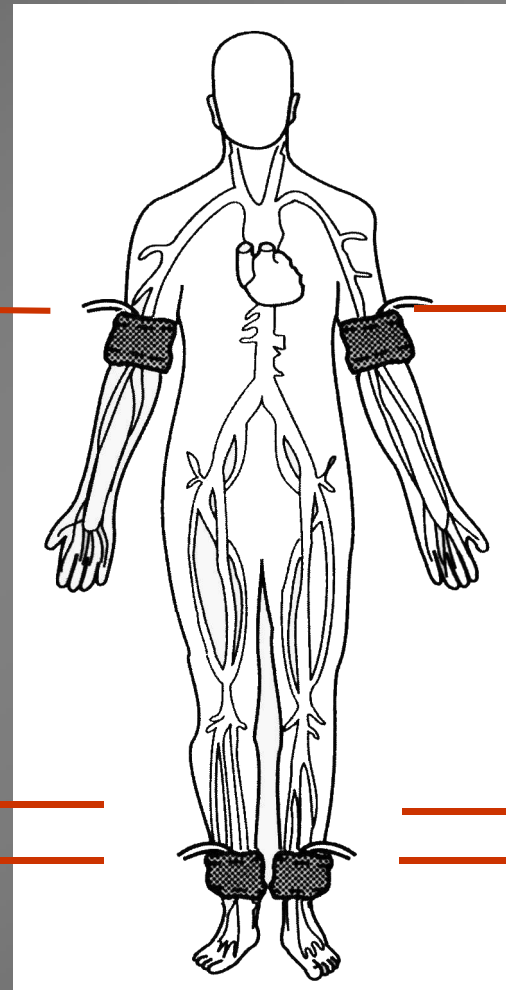
- Ankle-brachial index
- Segmental limb pressures
- Pulse volume recordings
- Doppler velocity waveform analysis
- Functional testing
 - Treadmill exercise testing
- Duplex scanning
- Advanced imaging techniques

How to Perform and Calculate the ABI

≥ 1.0 — Normal
0.81-0.90 — Mild Obstruction
0.41-0.80 — Moderate Obstruction
 ≤ 0.40 — Severe Obstruction

Right Arm
Pressure:

Left Arm
Pressure:



Pressure:

PT

DP

Pressure:

PT

DP

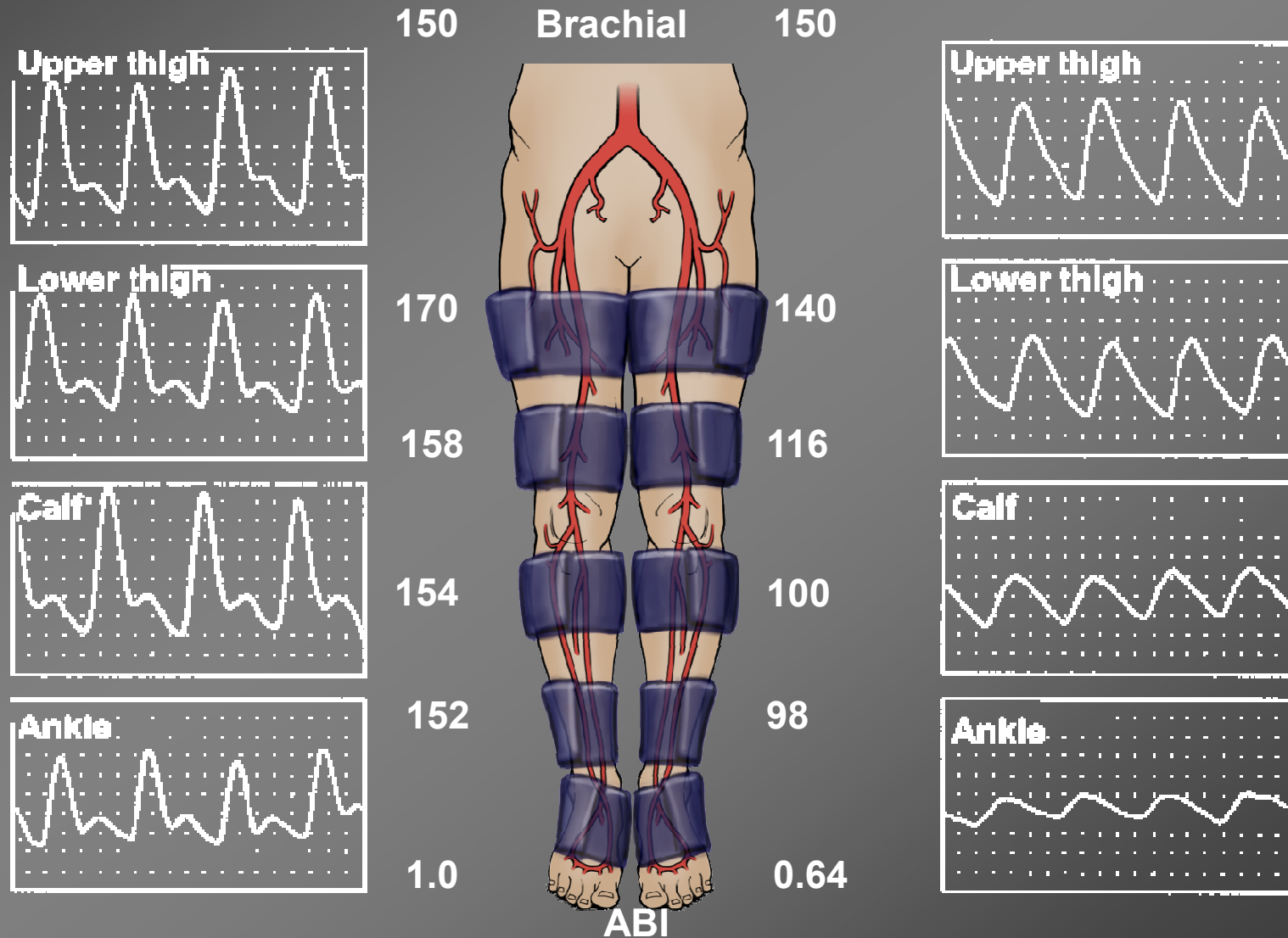
Right ABI

$\frac{\text{Higher Right Ankle Pressure}}{\text{Higher Arm Pressure}} = \frac{\text{mm Hg}}{\text{mm Hg}}$

Left ABI

$\frac{\text{Higher Left Ankle Pressure}}{\text{Higher Arm Pressure}} = \frac{\text{mm Hg}}{\text{mm Hg}}$

Segmental Limb Pressure and Pulse Volume Recordings



ACC/AHA 2005/2011 Guidelines

Diagnosis of PAD

I
B

MODIFIED

Use resting ankle brachial index (ABI) to establish lower extremity PAD diagnosis in those with suspected PAD, defined as individuals with 1 or more of the following: exertional leg symptoms, nonhealing wounds, age ≥ 65 years, or ≥ 50 years with a history of smoking or diabetes.

I
B

Use ABI to confirm and diagnosis and establish a baseline in all new patients with PAD, regardless of severity

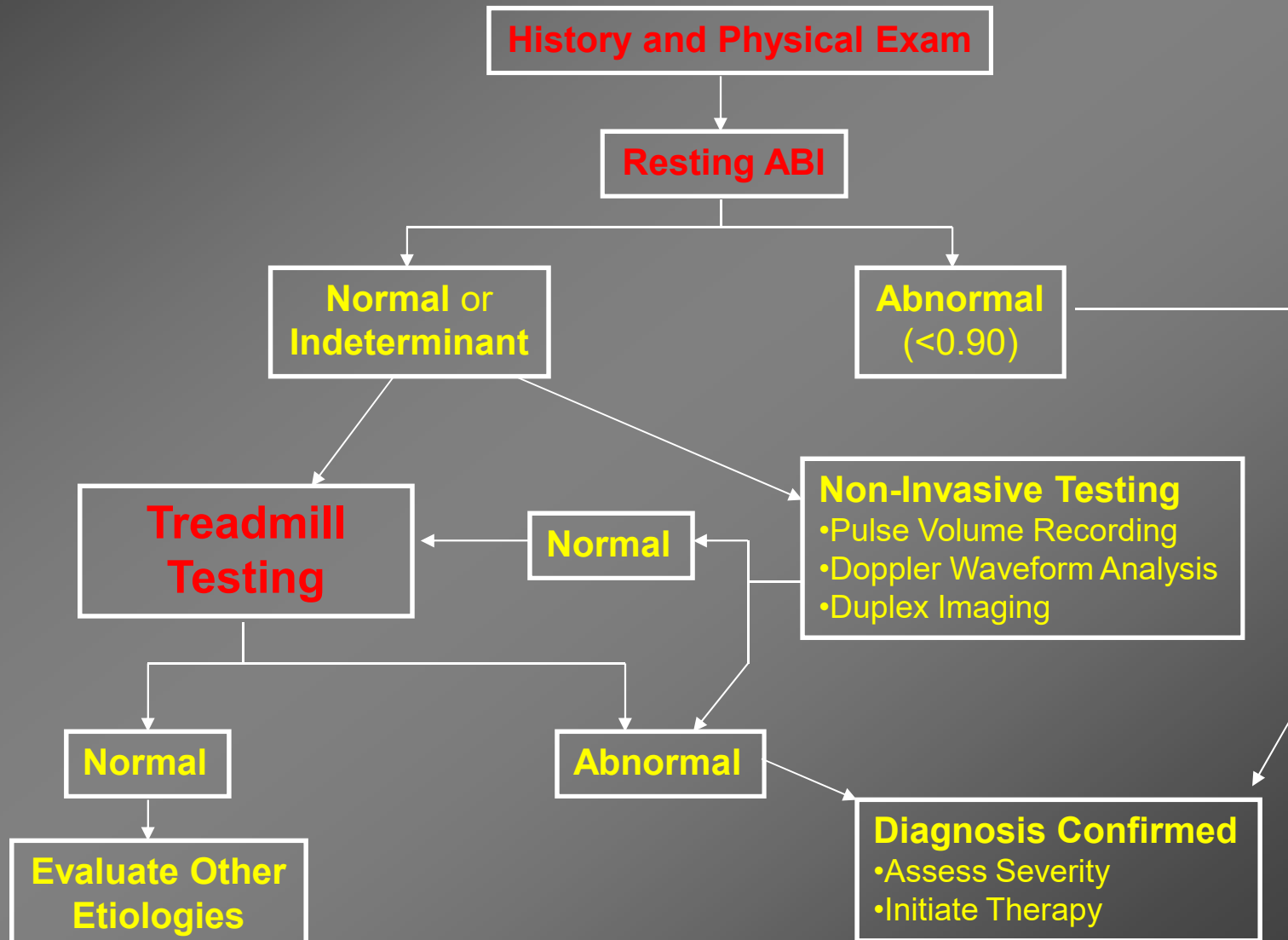
I
B

Use toe-brachial index to establish a diagnosis of PAD in those with non-compressible vessels

I
B

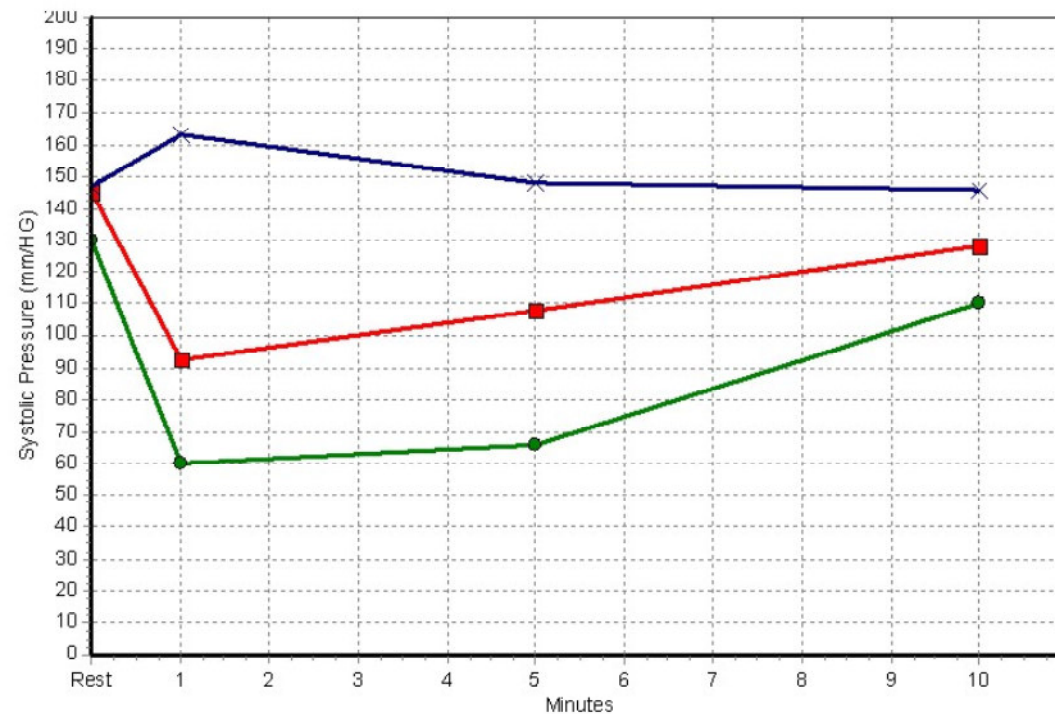
Segmental pressure measurements are useful to when anatomic localization of PAD is required to create a therapeutic plan

Establishing the Diagnosis of Intermittent Claudication



Post Exercise Ankle Pressures

	Rest	1	2	3	4	5	6	7	8	9	10
R Ankle (PT):	145	93				108					128
L Ankle (DP):	130	60				66					110
L Brachial:	147	163				148					146
R ABI	0.99	0.57				0.73					0.88
L ABI	0.88	0.37				0.45					0.75



Advanced Vascular Imaging

CT Angiography

- Maximum-intensity projection (MIPs)
 - Angiographic like representation
- Volume rendering
 - Preserves depth information
- Multi-planar reformat
- Curved planar reformat (CPR)
 - Perpendicular to median arterial centerline



MR Angiography

- Traditional: Time of flights
- Contrast-enhanced MRA
 - Improves speed of exam, anatomic coverage, and small- vessel resolution
- Time-resolved gadolinium enhanced sequences
 - Time-resolved imaging of contrast kinetics (TRICKS)
 - Provides angiographic like dynamic contrast passage
- Moving-table technique or multi-array, parallel-imaging
 - Optimize large field-of-view imaging

He is sent for ABI/PVR and arterial duplex revealing
ABI 0.5 on left with femoral-popliteal involvement
and an occluded bypass graft

What treatments should we offer to those with
intermittent claudication?

Treatment of PAD

Therapies Based Upon Symptoms

Intermittent Claudication

- Exercise Therapy
- Drugs
 - Pentoxifylline
 - Cilostazol
- Revascularization
 - *Severe disability*

Goal to provide relief of symptoms

Critical limb ischemia

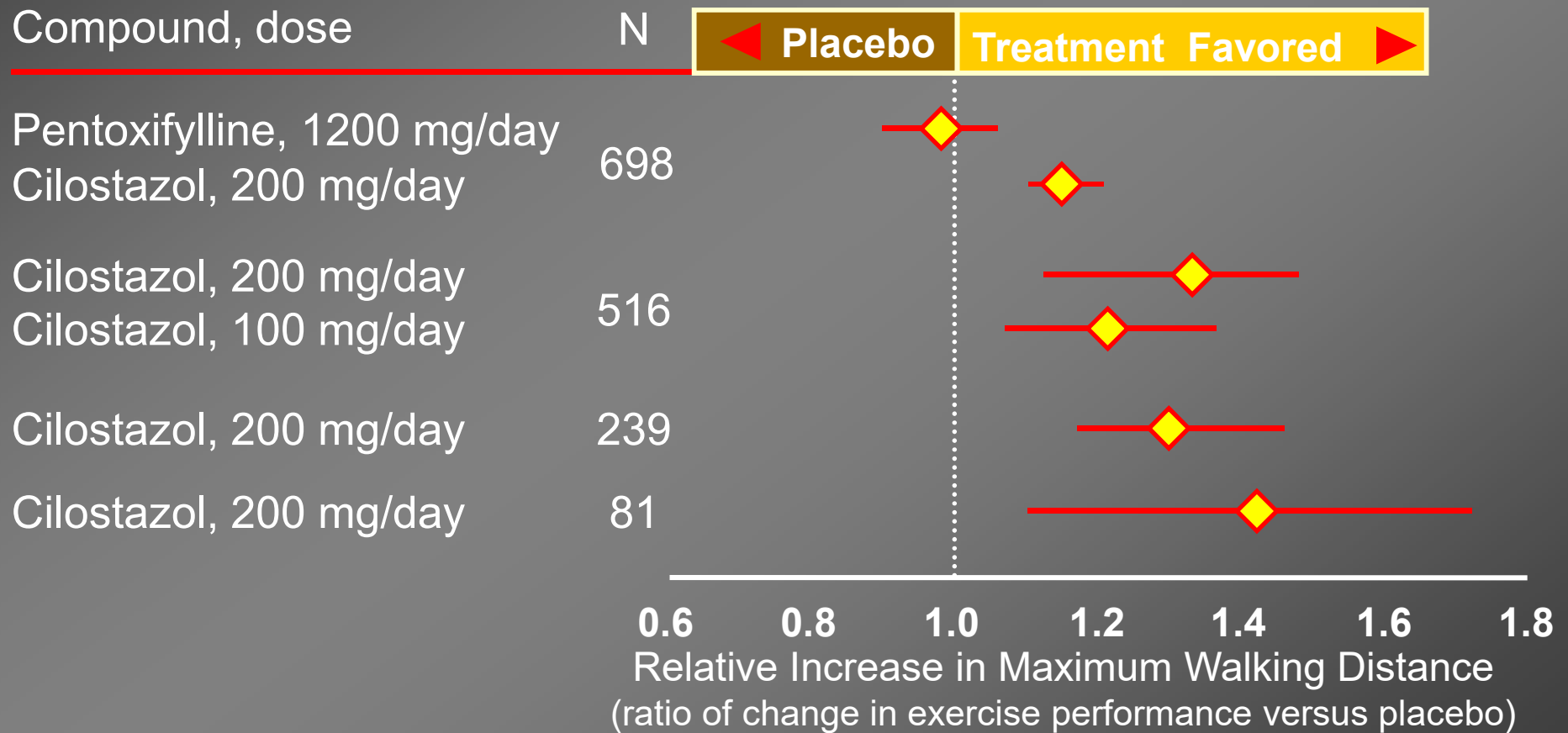
- Wound care
- Antibiotics
- Revascularization
 - Endovascular
 - Surgery

Goal to promote limb survival

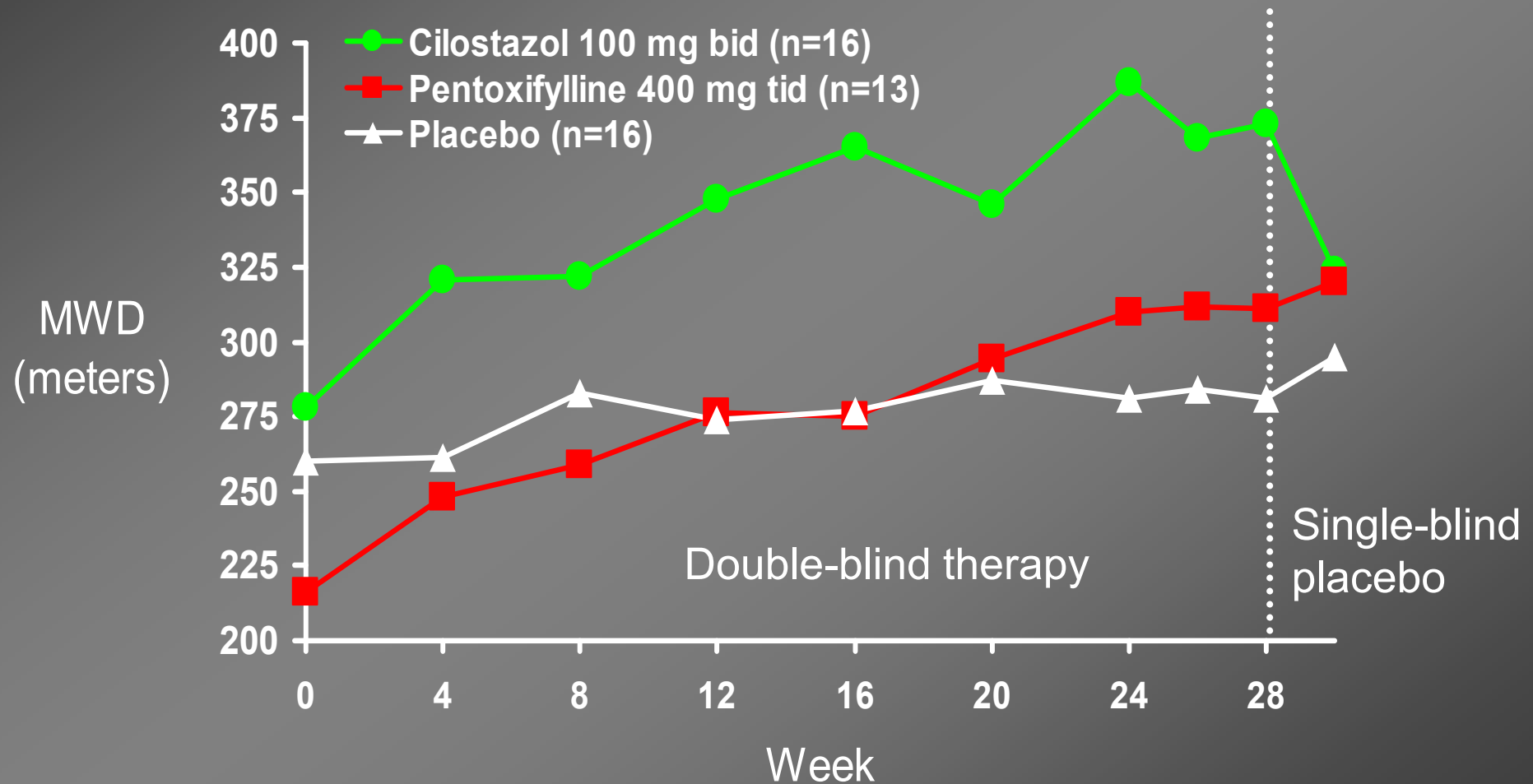
Treatment of PAD

Effect of Drug Therapy on Walking Distance

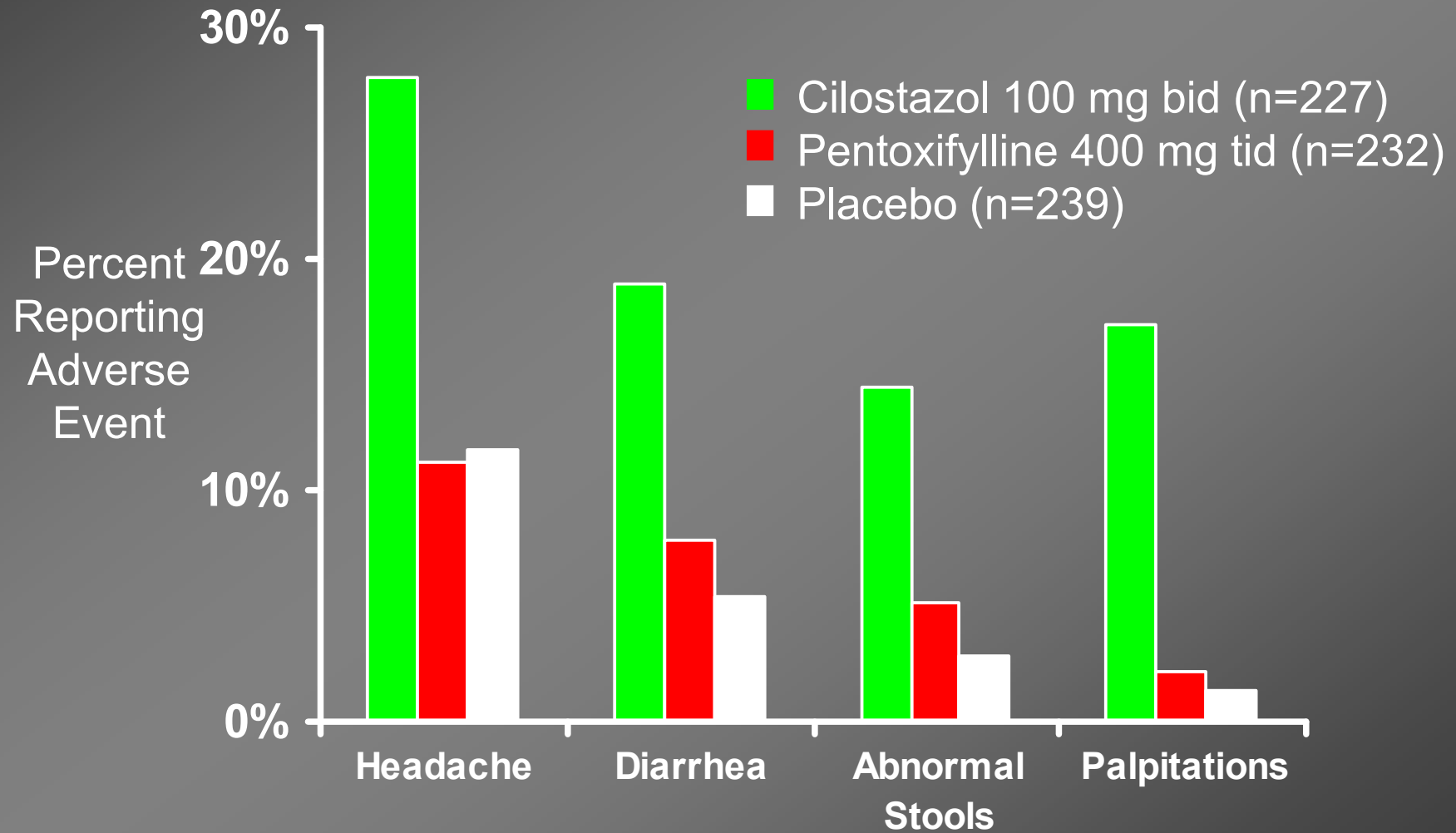
Meta-analysis of 4 randomized, placebo-controlled trials



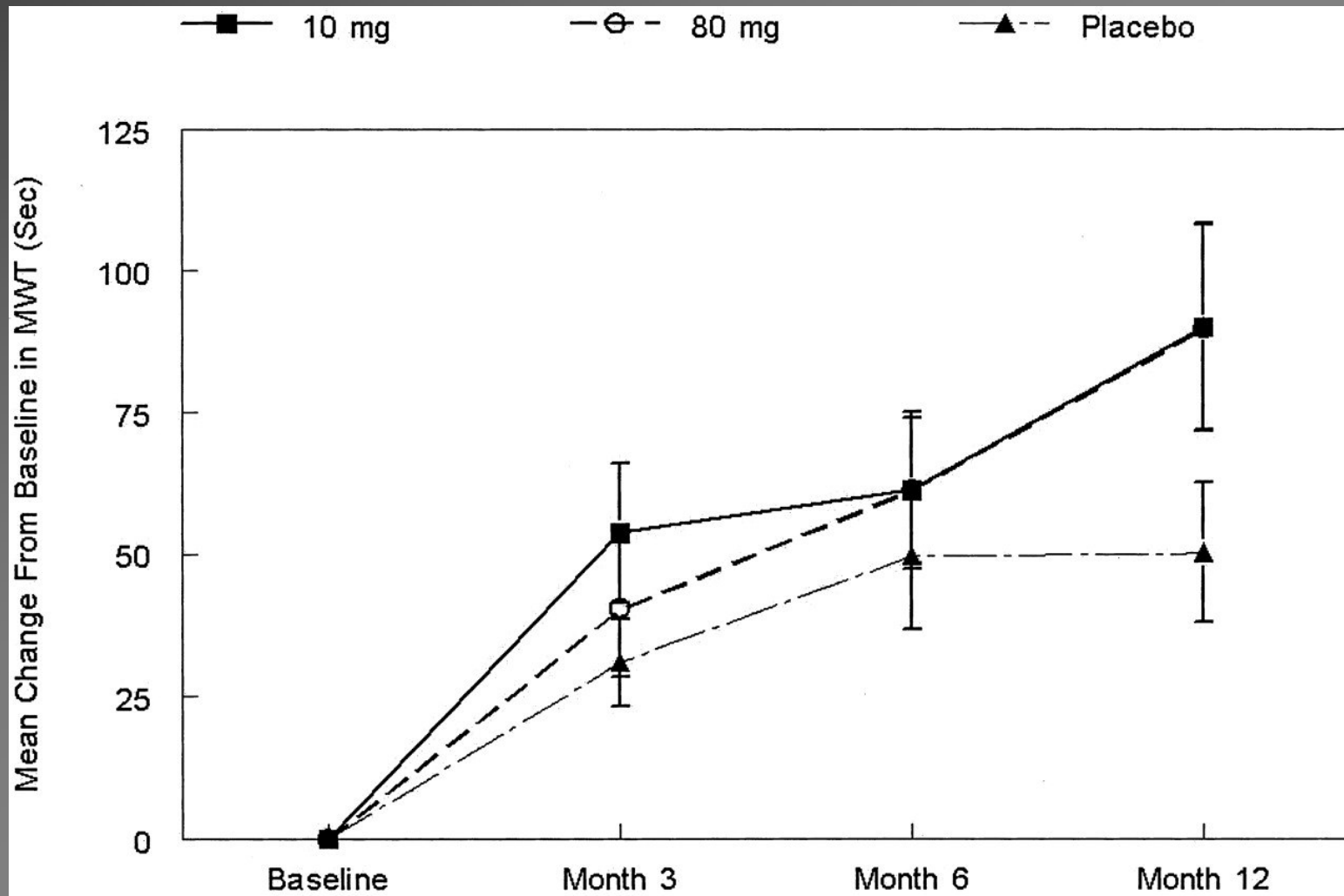
Maximal Walking Distance Before and After Drug Withdrawal



Most Common Adverse Event

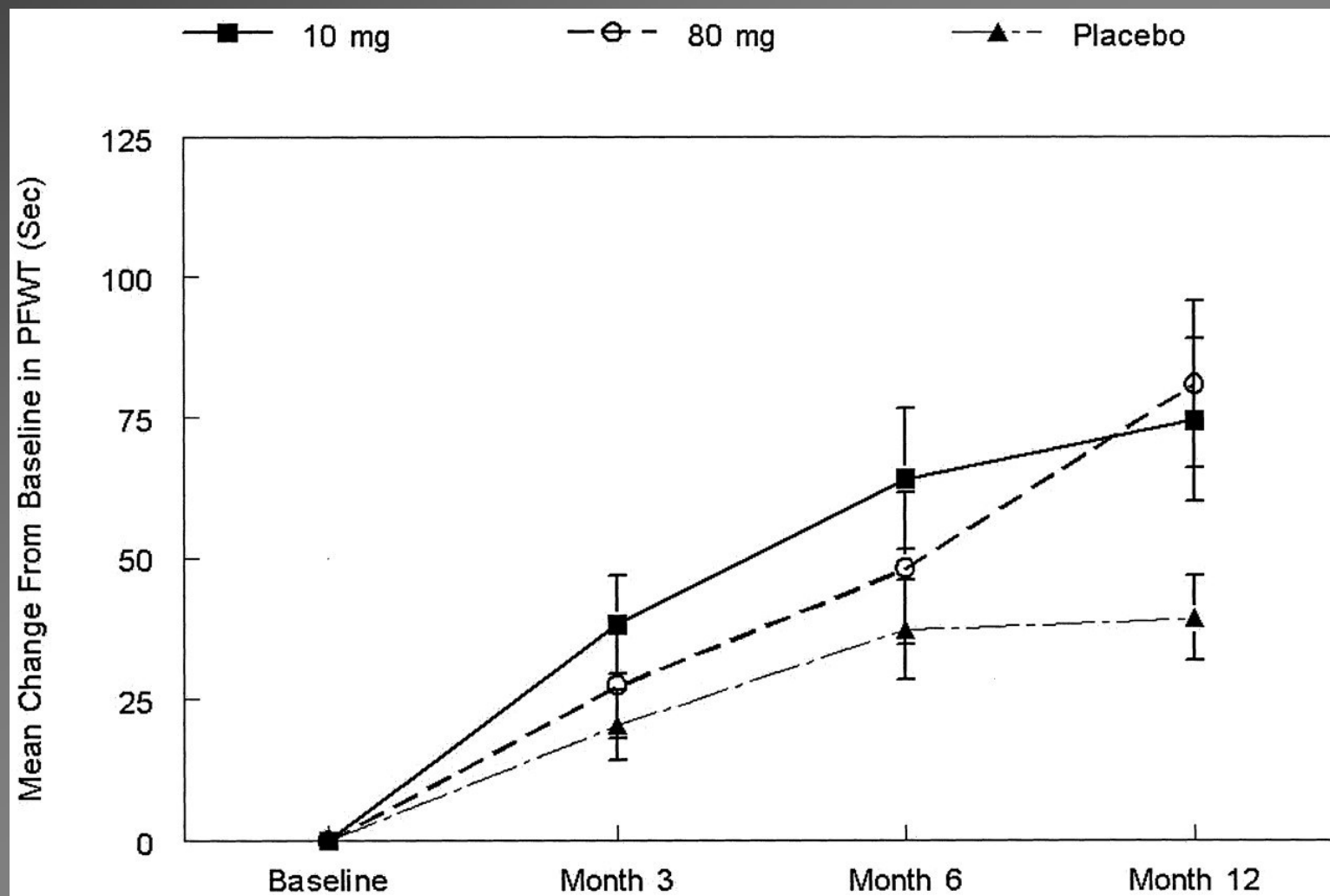


Effect of Atorvastatin of Maximum Walking Time in PAD



Mohler E R et al. Circulation 2003;108:1481-1486

Effect of Atorvastatin of Pain-Free Walking Time in PAD



Mohler E R et al. Circulation 2003;108:1481-1486

Effects of ACE inhibition on Claudication

Outcome Measure	No. of Participants	value		mean (95% CI) ^a		P Value ^c
		Baseline	6 mo	Within-Group Changes	Between-Group Difference	
Primary outcome measures, mean (SD)						
PFWT, s						
Placebo	106	142 (54)	156 (57)	14 (6 to 21)	75 (60 to 89)	<.001
Ramipril	106	140 (61)	229 (85)	88 (76 to 101)		
MWT, s						
Placebo	106	238 (71)	259 (80)	23 (13 to 36)	255 (215 to 295)	<.001
Ramipril	106	234 (91)	512 (235)	277 (238 to 316)		
Secondary outcome measures, limiting-leg ABI, mean (SD)						
At rest						
Placebo	106	0.55 (0.14)	0.54 (0.16)	0.00 (-0.02 to 0.02)	0.10 (0.08 to 0.13)	<.001
Ramipril	106	0.57 (0.14)	0.64 (0.13)	0.08 (0.06 to 0.09)		
Following exercise						
Placebo	106	0.43 (0.12)	0.42 (0.16)	0.00 (-0.03 to 0.18)	0.11 (0.08 to 0.14)	<.001
Ramipril	106	0.45 (0.14)	0.52 (0.14)	0.07 (0.05 to 0.09)		
WIQ scores, median (IQR)^d						
Distance score						
Placebo	106	6.1 (2.7 to 11.2)	4.7 (2.3 to 7.4)	-1.1 (-4.2 to 0.0)	13.8 (12.2 to 15.5)	<.001 ^e
Ramipril	106	6.3 (3.9 to 19.7)	16.9 (13.4 to 31.8)	9.9 (8.3 to 12.1)		
Speed						
Placebo	106	10.9 (6.5 to 17.4)	6.9 (3.3 to 10.9)	-3.3 (-4.0 to 0.0)	13.3 (11.9 to 15.2)	<.001 ^e
Ramipril	106	7.6 (6.5 to 14.4)	20.1 (15.2 to 30.2)	10.9 (7.6 to 12.0)		
Stair climbing						
Placebo	106	16.8 (15.3 to 38.7)	16.7 (12.6 to 21.0)	-4.2 (-8.4 to 0.0)	25.2 (25.1 to 29.4)	<.001 ^e
Ramipril	106	16.8 (15.7 to 37.8)	41.9 (31.0 to 67.1)	20.9 (16.8 to 25.2)		

Additional Effects of ACE Inhibition in PAD

SF-36 scores, median (IQR) ^a						
Physical Component Summary						
Placebo	106	31.4 (30.9 to 32.7)	32.5 (31.8 to 33.0)	0.2 (-0.4 to 1.8)]	8.2 (3.6 to 11.4) .02 ^e
Ramipril	106	32.3 (30.4 to 33.1)	41.4 (32.8 to 48.6)	6.3 (0.0 to 19.0)		
Mental Component Summary						
Placebo	106	47.8 (34.7 to 64.3)	48.5 (33.2 to 66.8)	0.1 (-0.5 to 0.3)]	0.5 (-0.7 to 1.1) .74 ^e
Ramipril	106	44.1 (33.7 to 62.2)	49.2 (35.1 to 62.5)	1.8 (0.0 to 3.9)		
Volume flow, limiting-leg ABI, mL/min						
Site of stenosis						
Placebo	50	602 (95)	633 (96)	31 (17 to 45)]	-2 (-27 to 22) .85
Ramipril	61	503 (140)	536 (148)	33 (14 to 53)		
Patent site						
Placebo	50	599 (118)	577 (109)	-22 (-29 to -16)]	63 (55 to 71) <.001
Ramipril	61	497 (67)	538 (72)	41 (36 to 46)		
Common femoral artery diameter, limiting leg, cm						
Site of stenosis						
Placebo	50	8.75 (0.52)	8.46 (0.53)	-0.12 (-0.15 to 0.31)]	0.22 (0.12 to 0.46) .44
Ramipril	61	6.81 (1.22)	6.43 (1.35)	0.33 (-0.02 to 0.54)		
Patent site						
Placebo	50	9.88 (0.60)	9.67 (0.60)	-0.13 (-0.18 to 0.42)]	0.12 (0.01 to 0.24) .23
Ramipril	61	8.70 (0.62)	8.86 (0.59)	0.16 (0.08 to 0.38)		

Exercise for PAD?

Your legs hurt when you walk so
go out and walk?

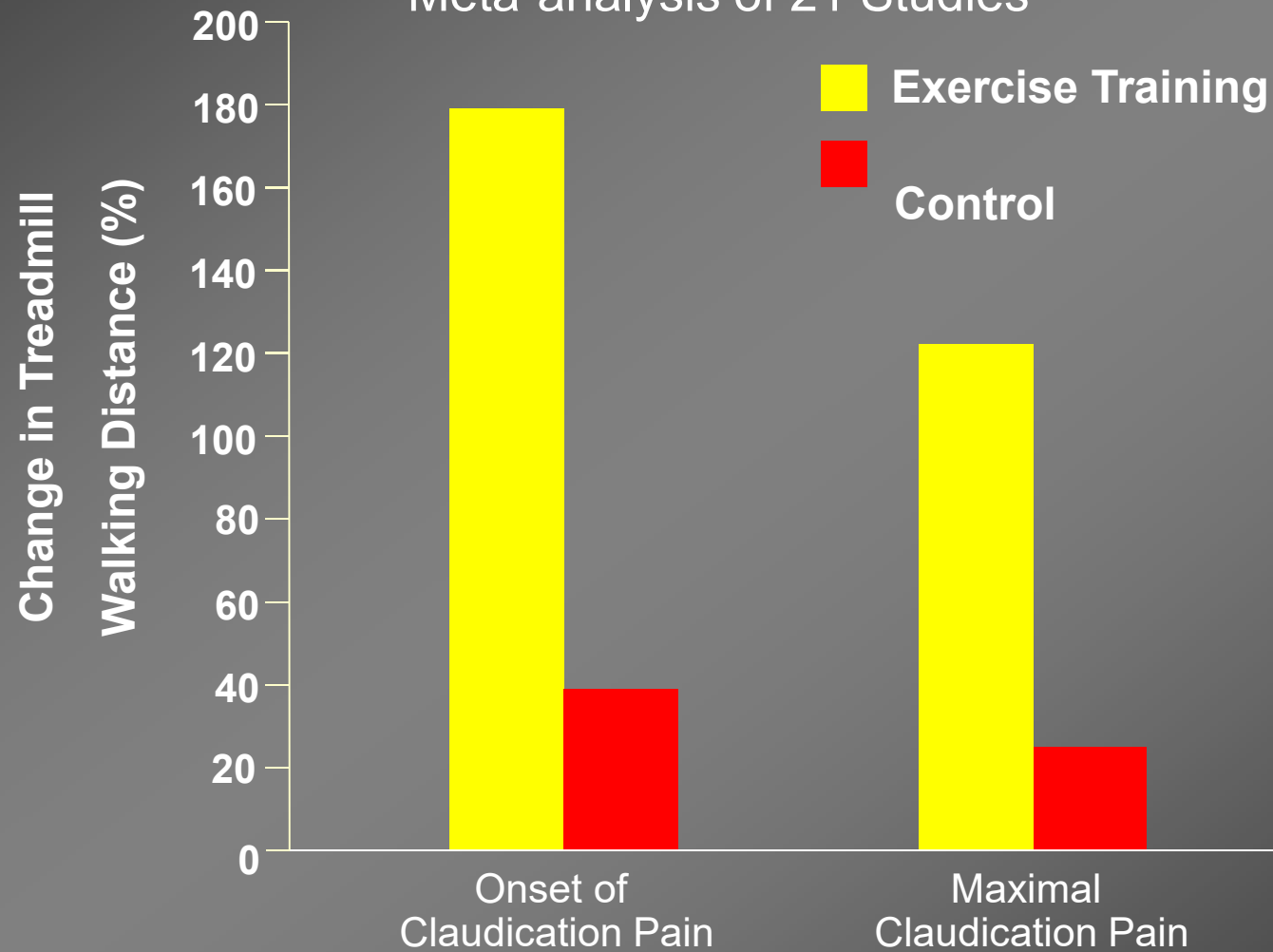
Effect of Exercise Training on Walking Ability in PAD



Treatment of PAD

Effect of Exercise Training

Meta-analysis of 21 Studies



Treatment of PAD

Effect of Exercise Components on Walking Distance

Exercise Duration	< 30 min/session	144 ± 419
	≥ 30 min/session	653 ± 364 *
Exercise Frequency	< 3 session/wk	249 ± 350
	≥ 3 sessions/wk	541 ± 263 *
Length of Program	< 26 weeks	275 ± 228
	≥ 26 weeks	519 ± 409 *
Training End Point	Onset of Pain	196 ± 78
	Near-Maximal Pain	607 ± 427 *
Mode of Exercise	Walking	512 ± 483 *
	Combination	287 ± 127

* $P < 0.05$

ACC/AHA 2005 Guidelines

Treatment of Claudication

Exercise



Supervised exercise training should be the initial treatment

- 30-45 minute sessions
- 3 or more times per week
- At least 12 weeks



Value of unsupervised exercise programs is not well established

Drug therapy



Cilostazol 100 mg twice daily

- Can improve symptoms & increase walking distance
- Indicated for lifestyle-limiting claudication
- Contraindicated in patients with heart failure

- Pentoxifylline 400 mg three daily



Consider as an alternative to cilostazol



Effectiveness of pentoxifylline is marginal and not well established

Revascularization for Aorto-Iliac Arterial Disease

Aortofemoral Bypass

- Primary patency at 5 years of 81-85%¹
- Perioperative mortality 5-8%¹
- Reserved for severe diffuse disease cases²
- Indicated for Rutherford class ≥ 3 ²

Percutaneous Intervention

- Patency at 5 years of 65-80%¹
- Perioperative mortality 0.1%¹
- Treatment of choice³
- Indicated for Rutherford class ≥ 2 ²

1. Raptis S. et al. Eur. J. Vasc. Endovasc. Sur. 1995; 9: 97-102

2. Rosenfield K and Isner JM. Chap 97 in Textbook of Cardiovascular Medicine 1998

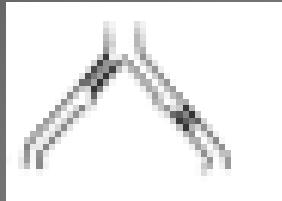
1. Becker GJ et al. Radiology 1989;170:921-940

2. Belli A-M et al. Clin Radiol 1990;41:380-3

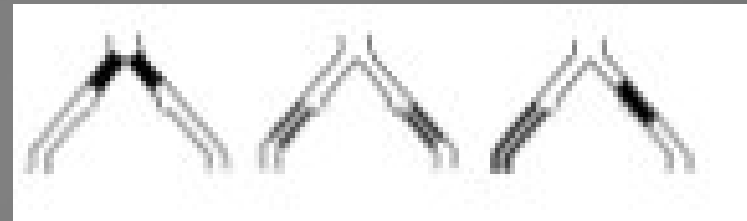
3. Rosenfield K and Isner JM. Chap97 in Textbook of Cardiovascular Medicine 1998

Lesion-guided approach for treatment of aorto-iliac disease

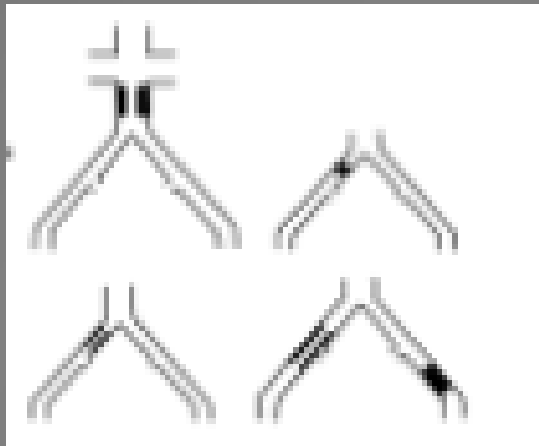
A
Endovascular
is procedure
of choice



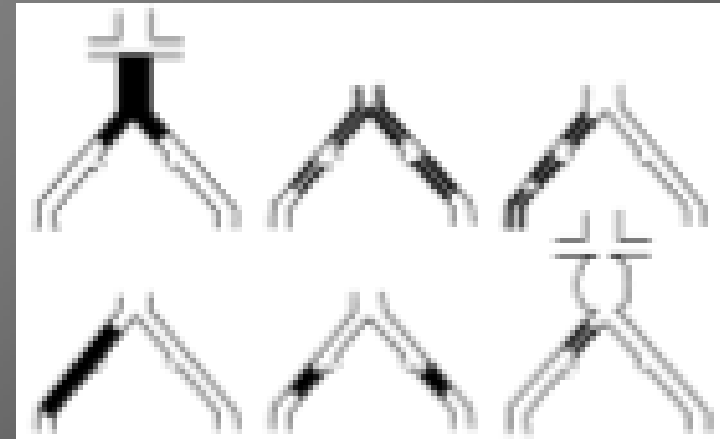
C
Surgery is
preferred for
good-risk



B
Endovascular
is preferred
therapy



D
Surgery is
procedure of
choice



Treatment of PAD

Revascularization for Femoro-Popliteal Disease

Femoro-Popliteal Bypass Surgery

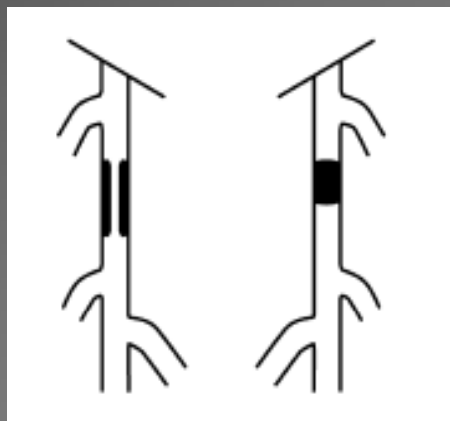
- Primary patency at 5 years of 60-80%
- Autologous veins preferred to synthetic grafts
- Perioperative mortality 0-3%
- Indicated for Rutherford class ≥ 3

Femoro-Popliteal Angioplasty

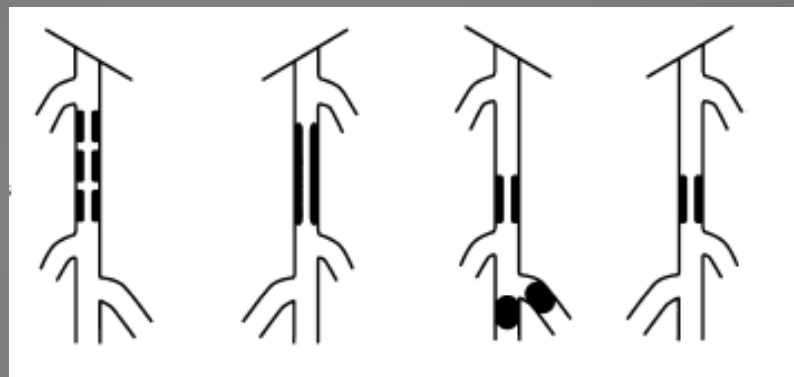
- Patency at 2-5 years ranges between 40-70%
- Technical problems due several anatomic issues:
 - Occlusions vs stenosis
 - Diffuse disease
 - Adductor canal
 - Disease in run off vessels
- Perioperative mortality is very low
- Indicated for Rutherford class ≥ 2

Lesion-guided approach for treatment of femoro-popliteal disease

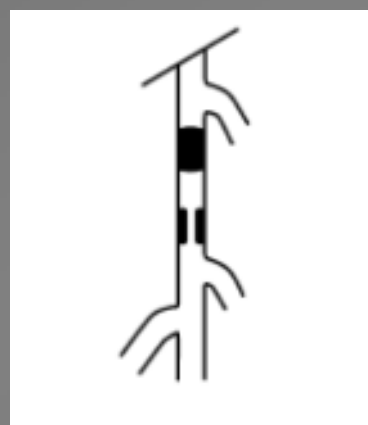
A
Endovascular
is procedure
of choice



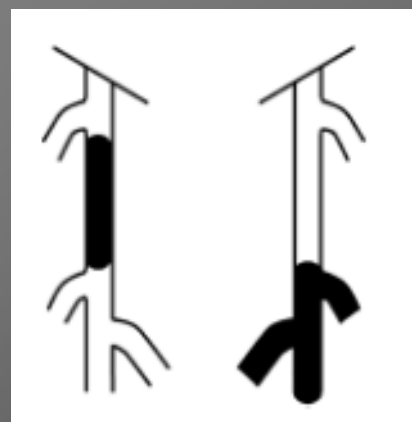
B
Endovascular
is preferred
therapy



C
Surgery is
preferred for
good-risk



D
Surgery is
procedure of
choice



ACC/AHA 2005 Guidelines

Treatment of Claudication

Endovascular therapies



Only indicated for patients with

- Vocational or lifestyle-limiting disability;
- Reasonable likelihood of symptomatic improvement;
- Prior failure of exercise or pharmacological therapy; and,
- Favorable risk-benefit ratio



Not indicated as a prophylactic treatment



Preferred method for revascularization of TASC type A iliac and femoropopliteal arterial lesions

Surgery



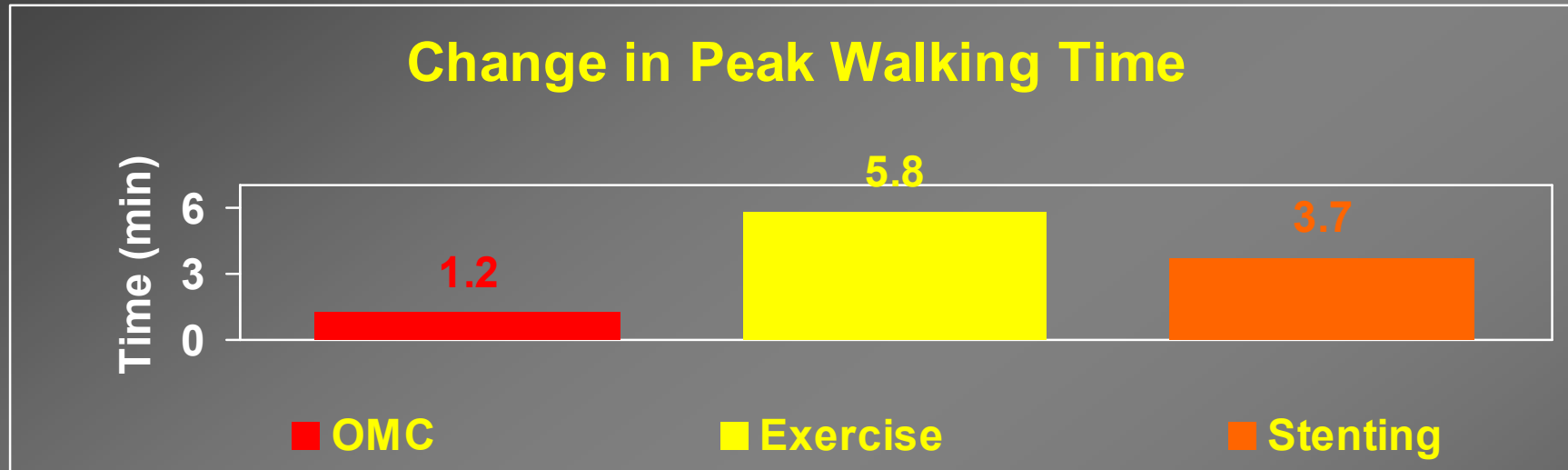
Indicated for patients

- With significant functional disability from symptoms
- Who are unresponsive to exercise or pharmacotherapy
- Who have a reasonable likelihood of symptomatic improvement



Surgical intervention is not indicated to prevent progression to limb-threatening ischemia

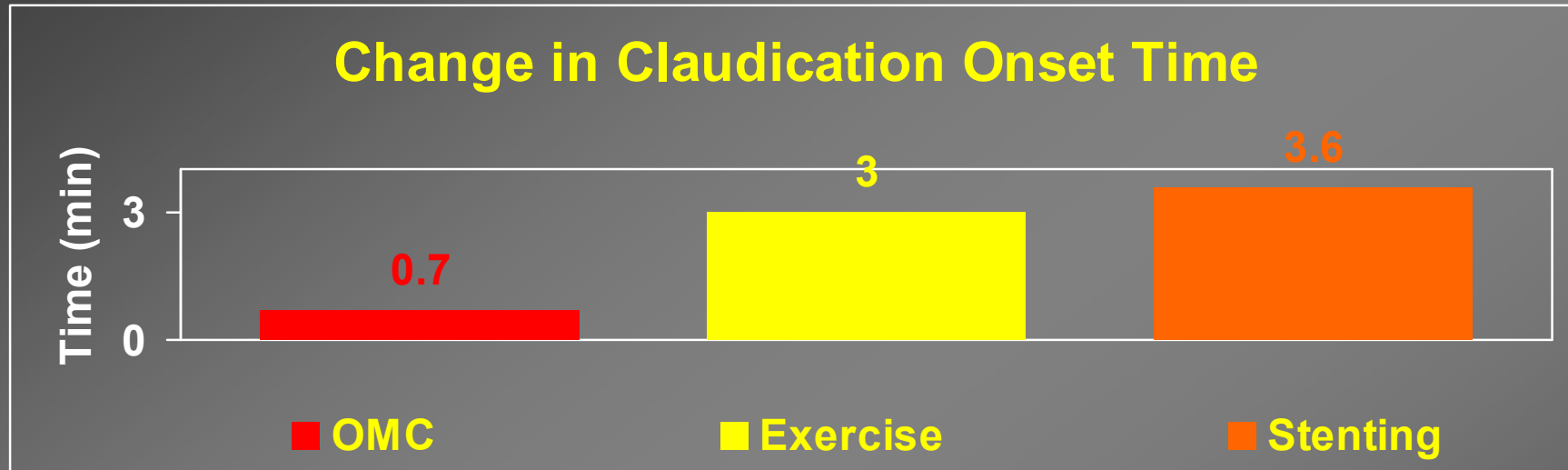
Exercise vs Stenting for Claudication



Pair-wise comparisons

	Difference (minutes)	<i>P</i> value
Exercise vs. OMC	4.6 (95% CI, 2.7-6.5)	<0.001
Stent vs OMC	2.5 (95% CI, 0.6-4.4)	0.02
Exercise vs Stenting	2.1 (95% CI, 0.0-4.2)	0.04

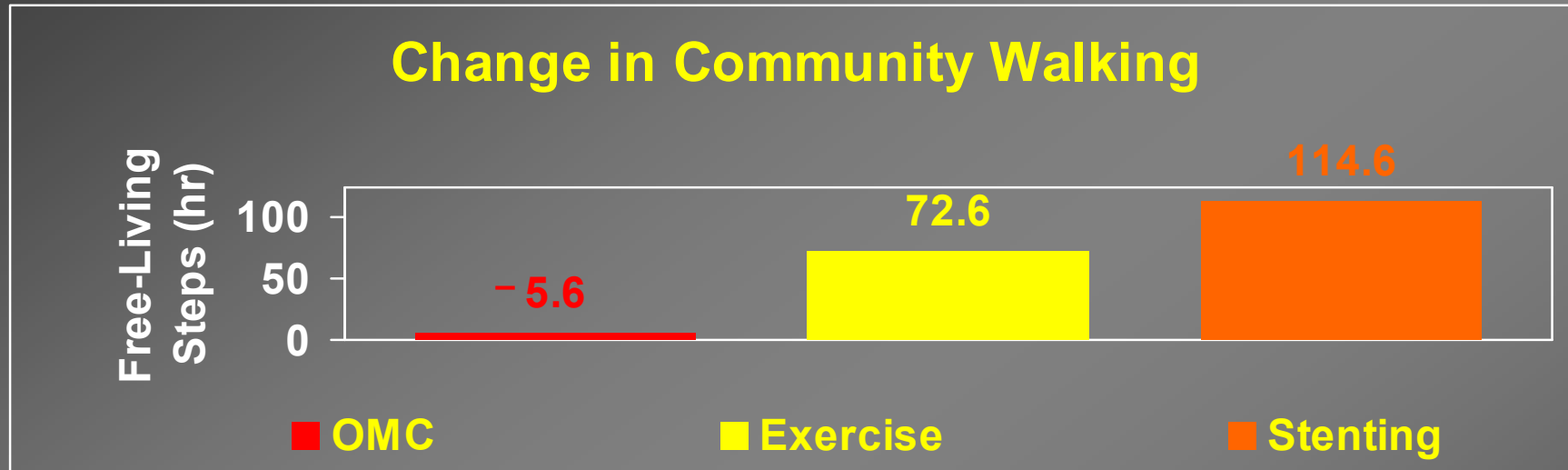
Exercise vs Stenting for Claudication



Pair-wise comparisons

	Difference (minutes)	<i>P</i> value
Exercise vs. OMC	2.2	<0.003
Stent vs OMC	2.9	0.006
Exercise vs Stenting	0.7	0.43

Exercise vs Stenting for Claudication

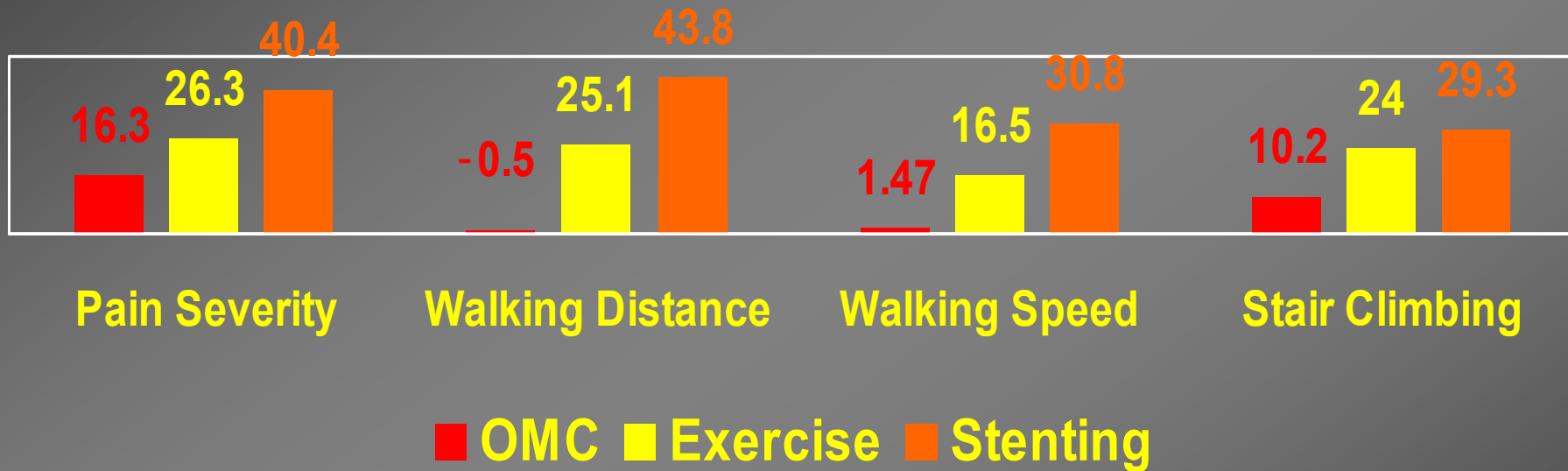


Pair-wise comparisons

	Difference (steps)	<i>P</i> value
Exercise vs. OMC	78	0.06
Stent vs OMC	120	0.10
Exercise vs Stenting	42	0.47

Exercise vs Stenting for Claudication

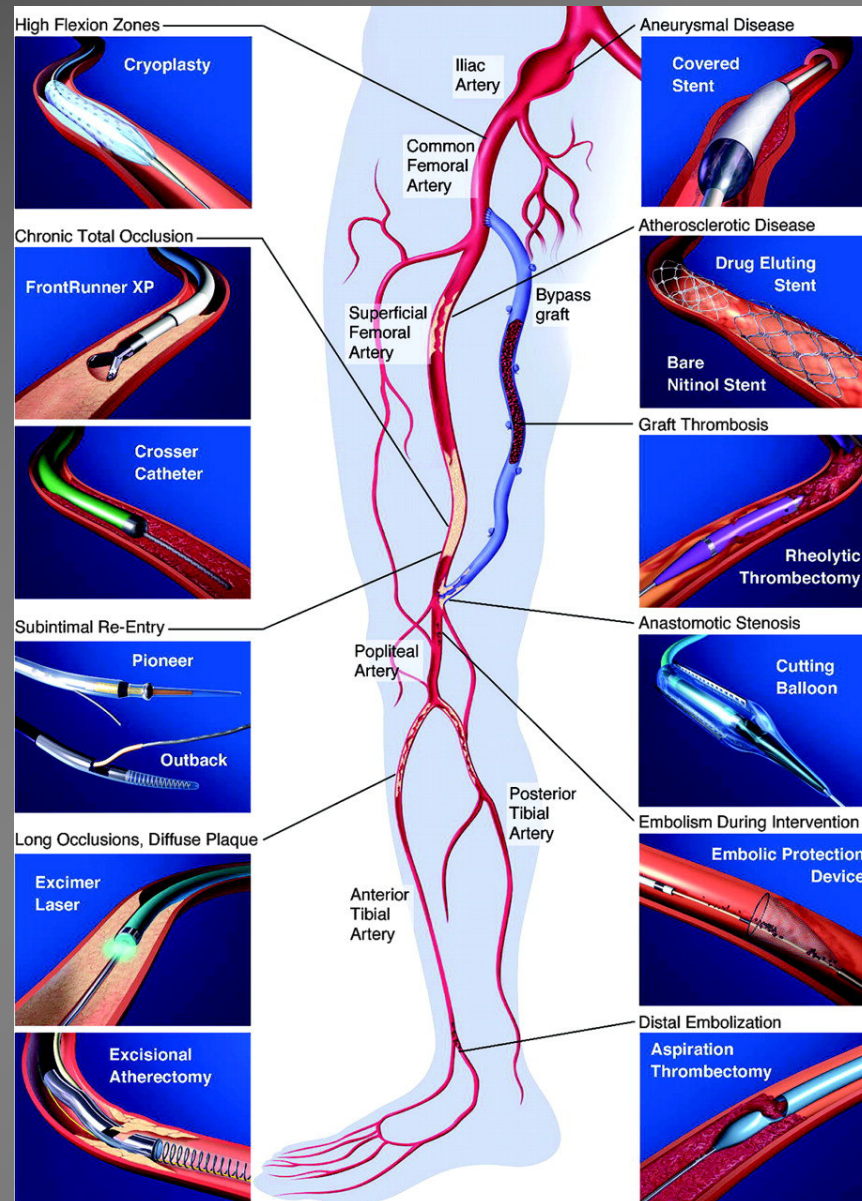
Change in WIQ



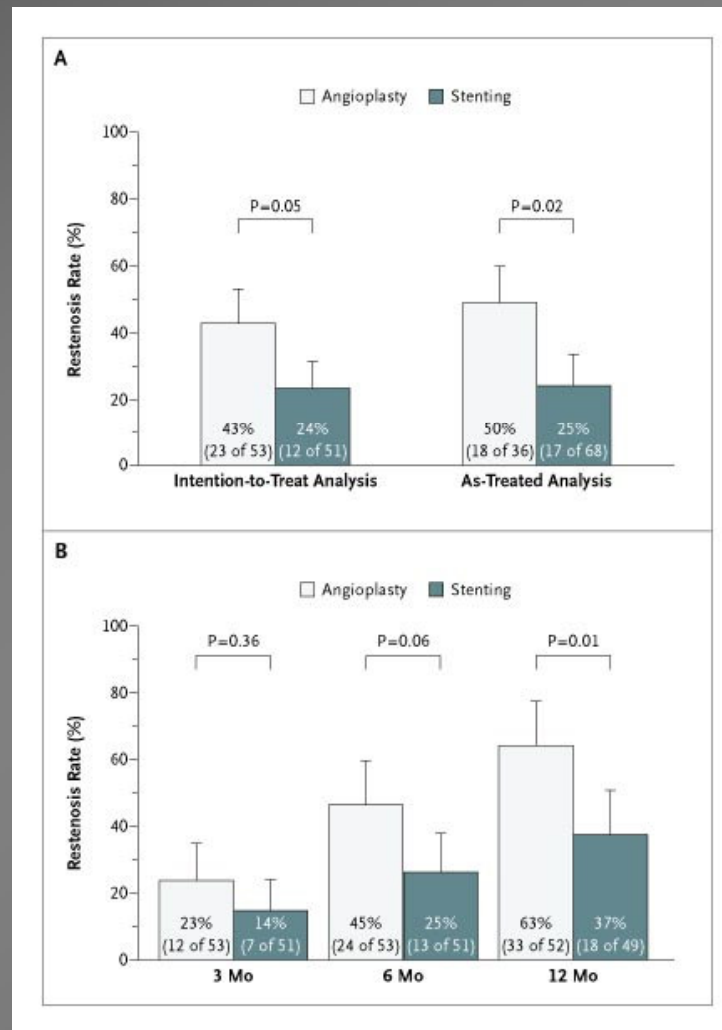
He is placed on cilostazol 100 mg twice daily and advised to perform interval exercise training but claudication remains at 1 block.

So what if initial treatment is inadequate?

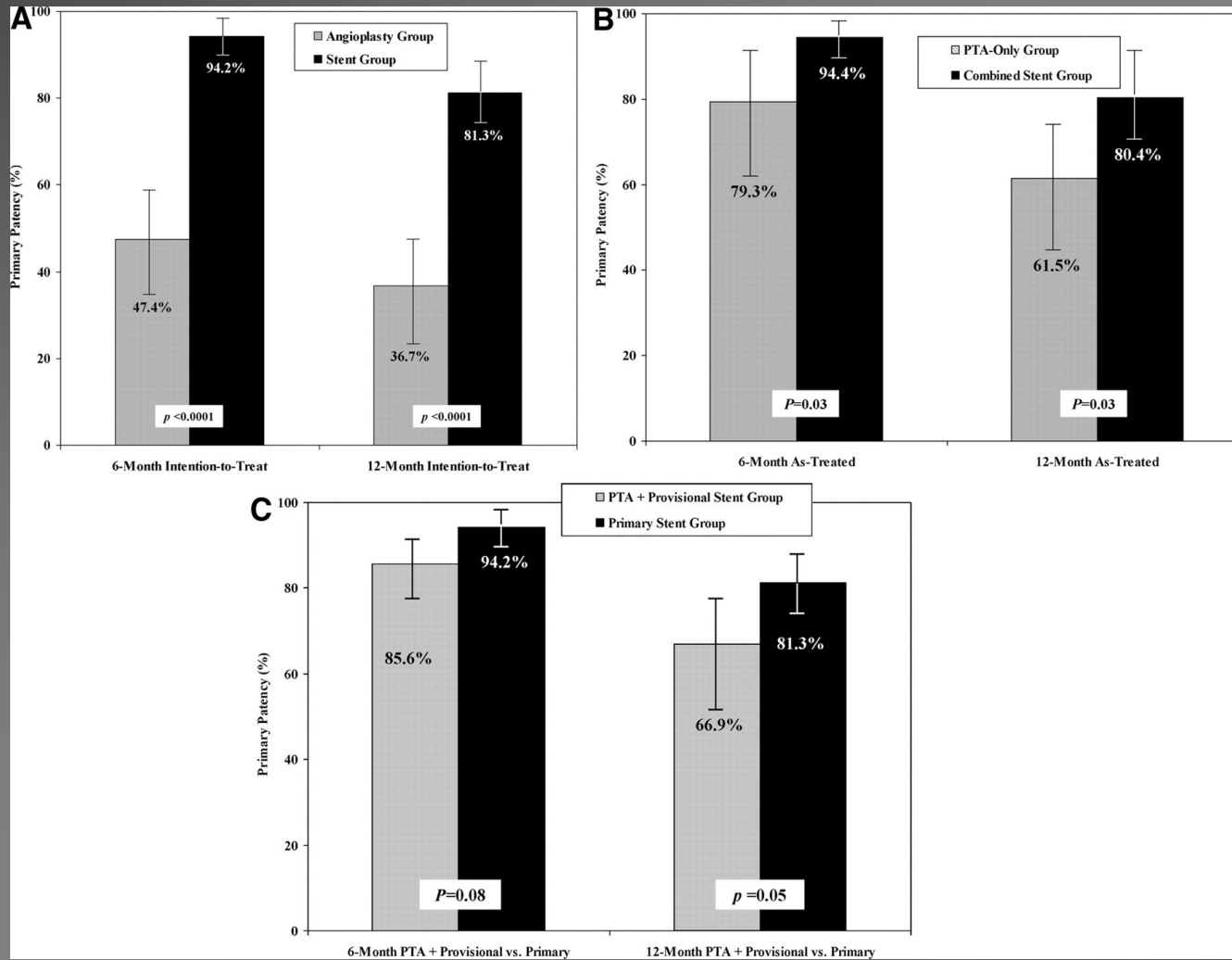
Overview of New Technologies



Angioplasty vs. Stent in the Superficial Femoral Artery

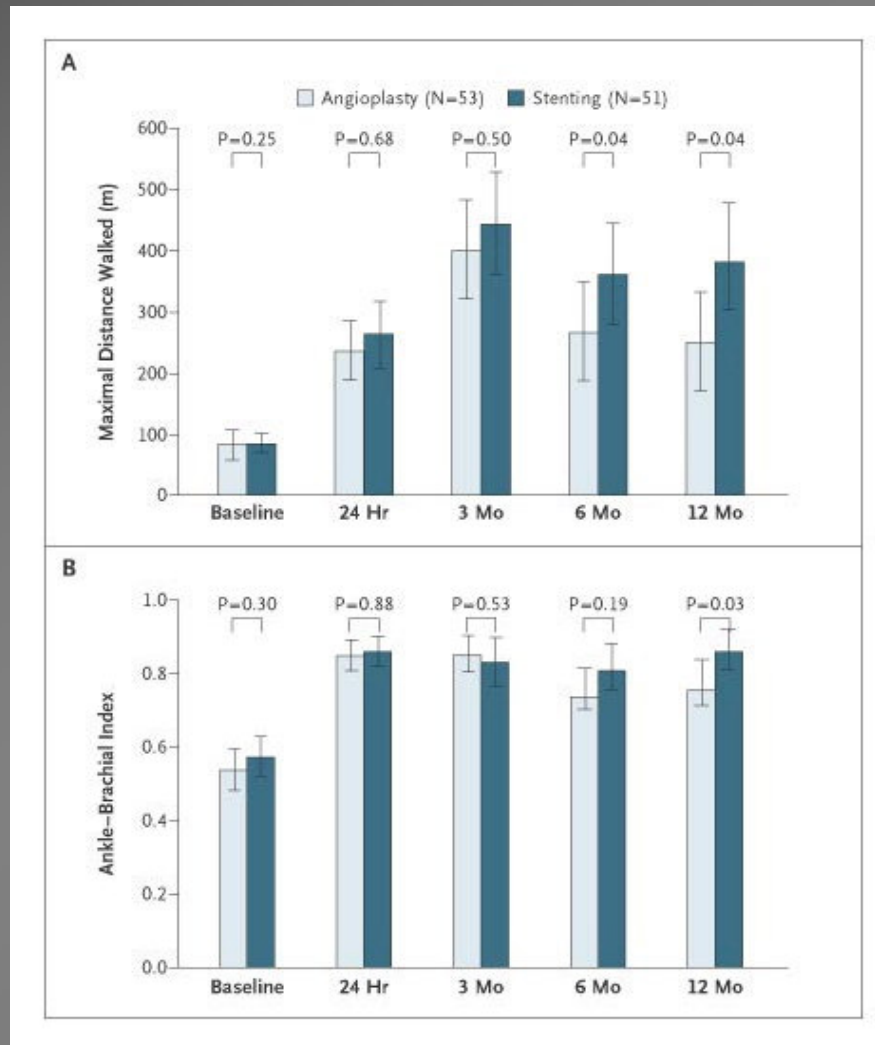


Primary Patency Femoral Angioplasty vs Stenting



Laird et al. Circ Cardiovasc Interv 2010;3:267-276

Clinical Effects of Primary Stenting vs Angioplasty for Femoral Dz

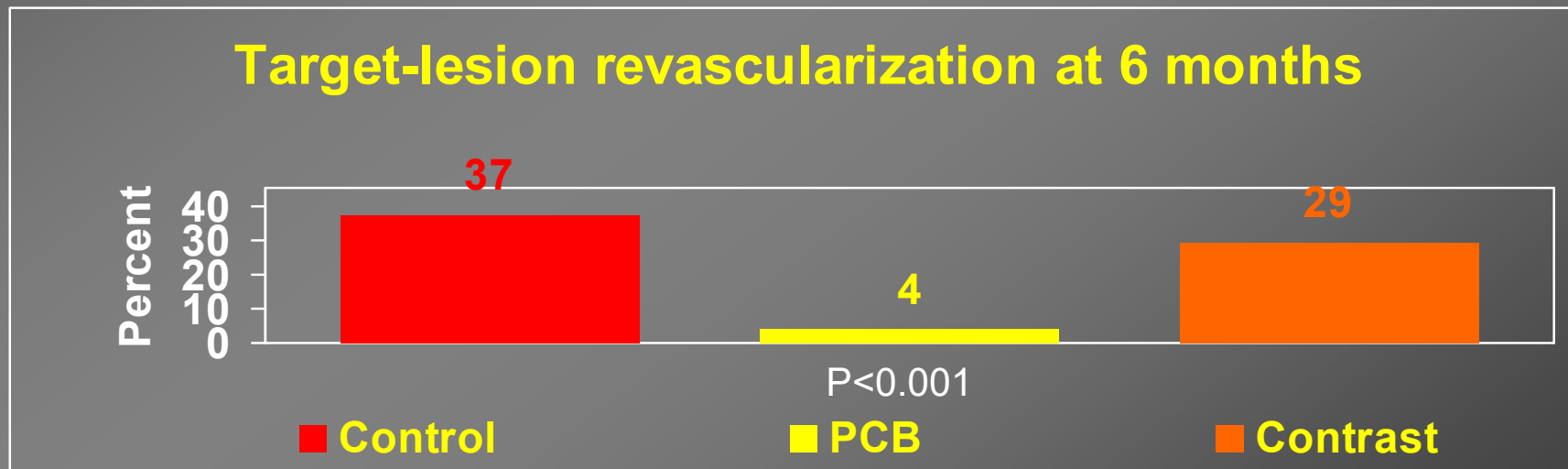
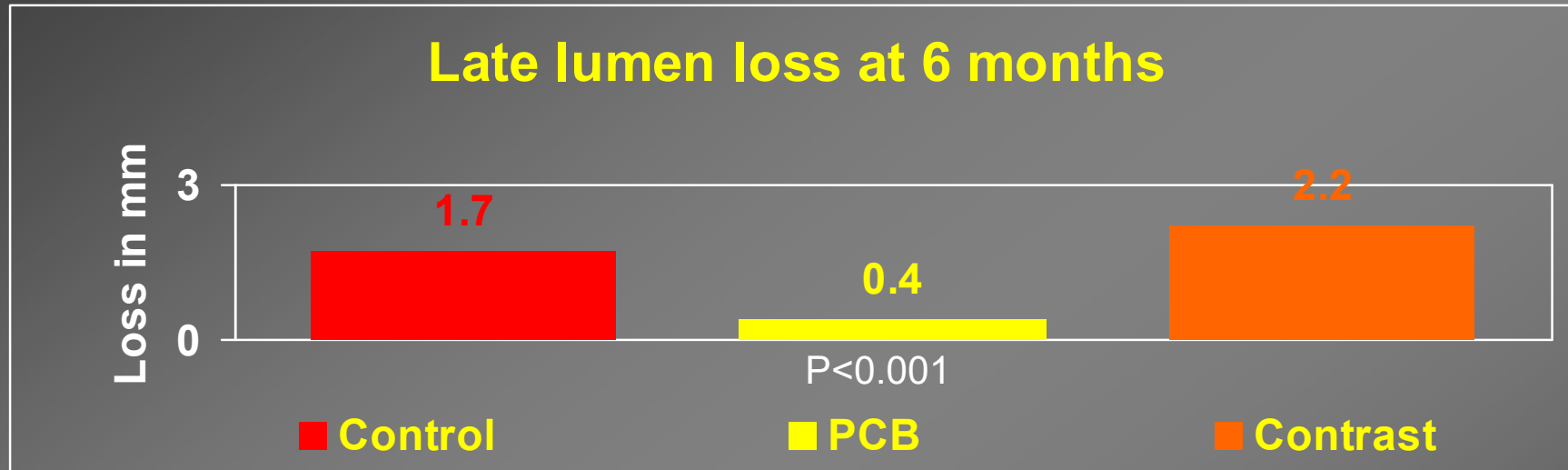


Schillinger et al. N Engl J Med 2006;354:1879-1888.



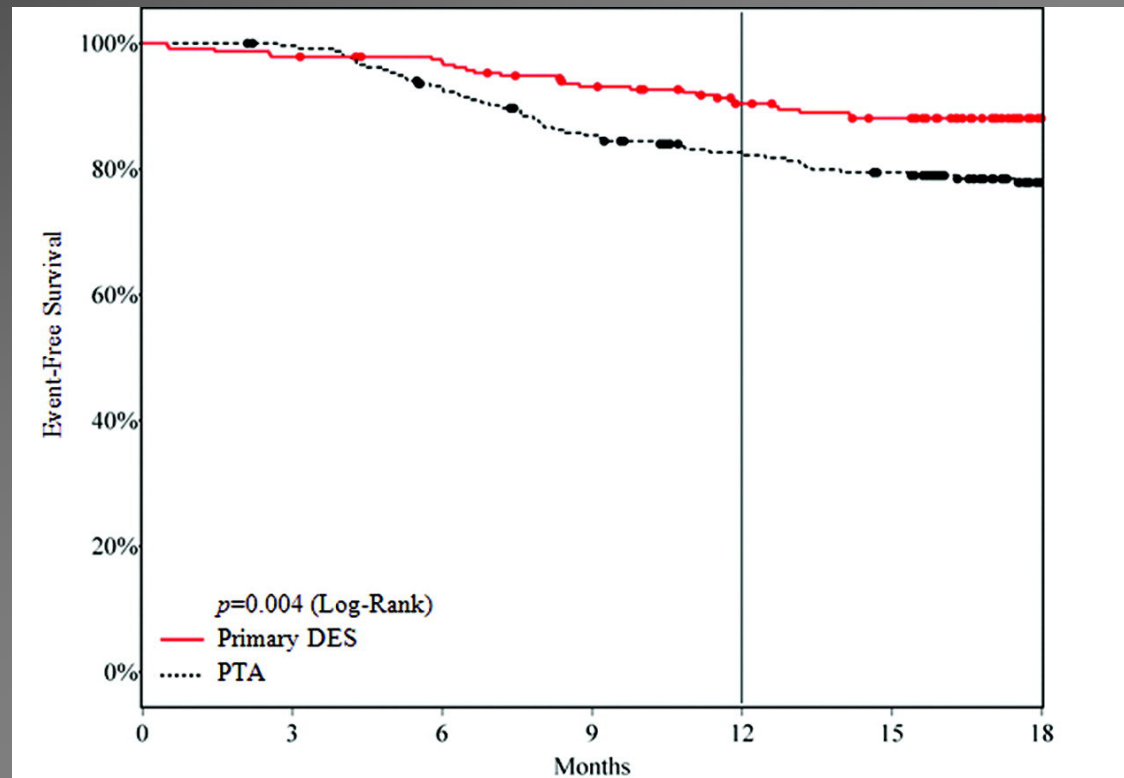
The NEW ENGLAND
JOURNAL of MEDICINE

Paclitaxel Coated Balloon for Femoropopliteal Dz



DES vs Angioplasty for Femoropopliteal Dz

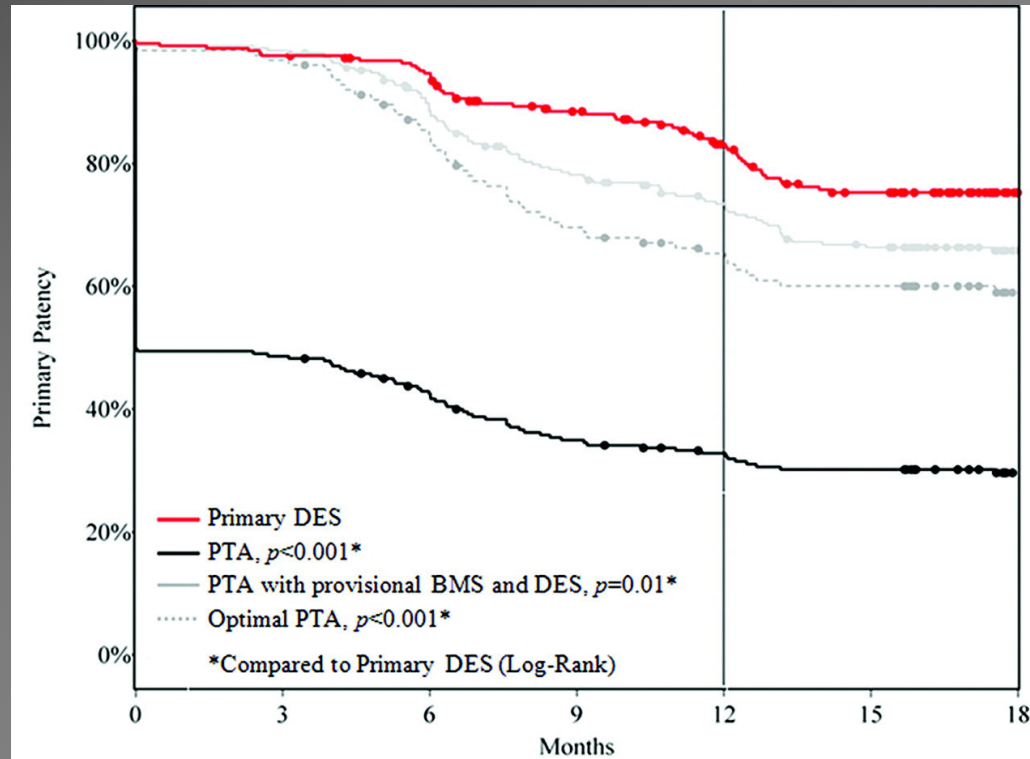
Zilver (Paclitaxel) Stent



Kaplan Meier Estimates of Event-Free Survival, Values Represent Patients								
Months Post-procedure	EFS \pm Standard Error		Cumulative Failed		Cumulative Censored		Remaining at Risk	
	PTA	Primary DES	PTA	Primary DES	PTA	Primary DES	PTA	Primary DES
0	100.0 \pm 0.0%	100.0 \pm 0.0%	0	0	0	0	236	235
1	100.0 \pm 0.0%	99.1 \pm 0.6%	0	2	0	0	236	233
6	93.2 \pm 1.7%	97.0 \pm 1.1%	16	7	5	3	215	225
12	82.6 \pm 2.5%	90.4 \pm 1.9%	40	22	15	16	181	197

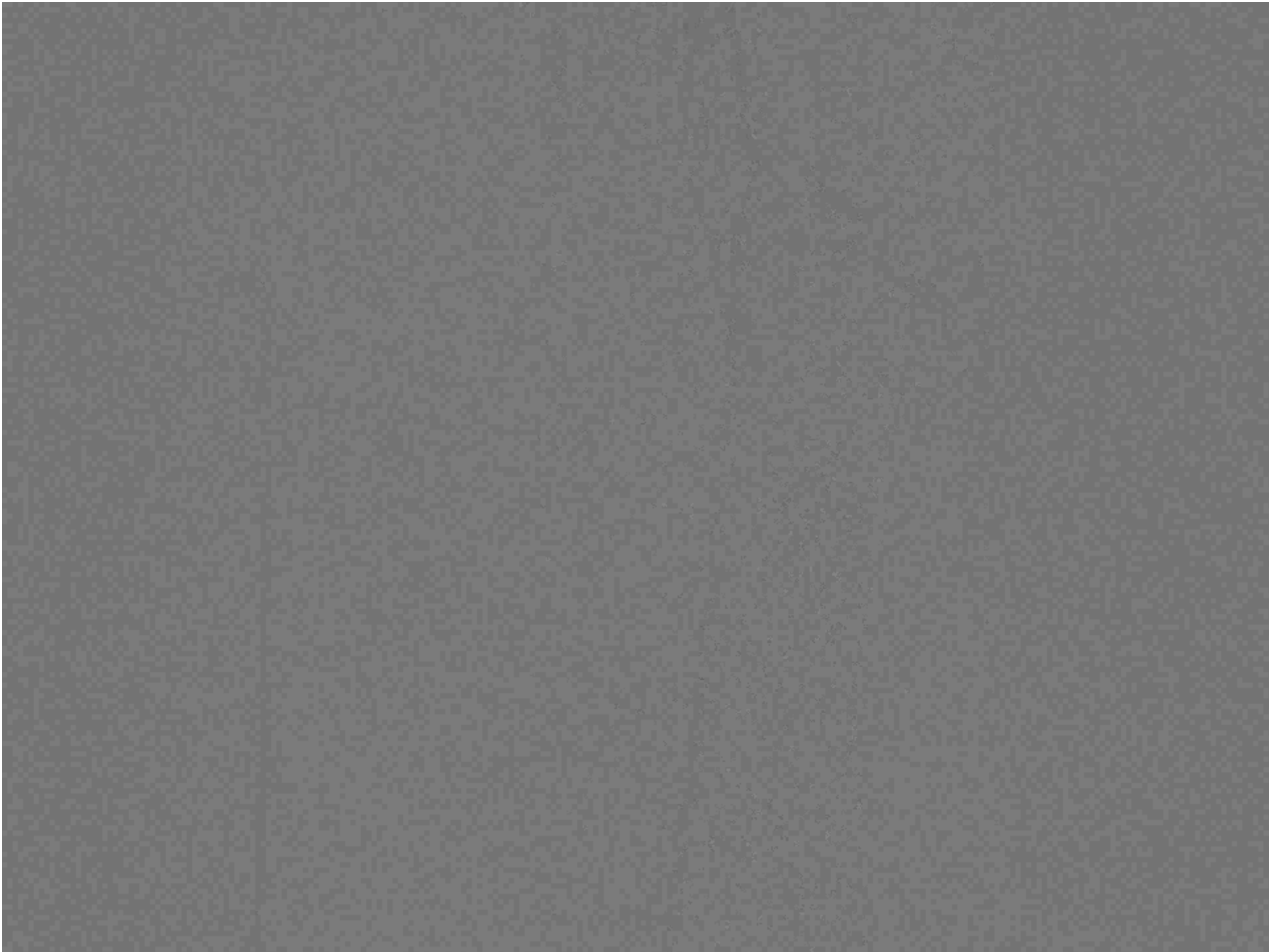
Dake M D et al. Circ Cardiovasc Interv 2011;4:495-504

DES vs Angioplasty for Femoropopliteal Dz *Zilver (Paclitaxel) Stent*



Kaplan Meier Estimates of Primary Patency, Values Represent Lesions

Months Post-procedure	Primary Patency \pm Standard Error		Cumulative Failed		Cumulative Censored		Remaining at Risk	
	PTA	Primary DES	PTA	Primary DES	PTA	Primary DES	PTA	Primary DES
0	49.8 \pm 3.2%	99.6 \pm 0.4%	126	1	0	0	125	246
1	49.4 \pm 3.2%	99.2 \pm 0.6%	127	2	0	0	124	245
6	42.5 \pm 3.1%	94.7 \pm 1.4%	144	13	5	3	102	231
12	32.8 \pm 3.0%	83.1 \pm 2.4%	167	40	10	26	74	181



101 | | | | 1151 | | | | 1201 | | | | 12

GI

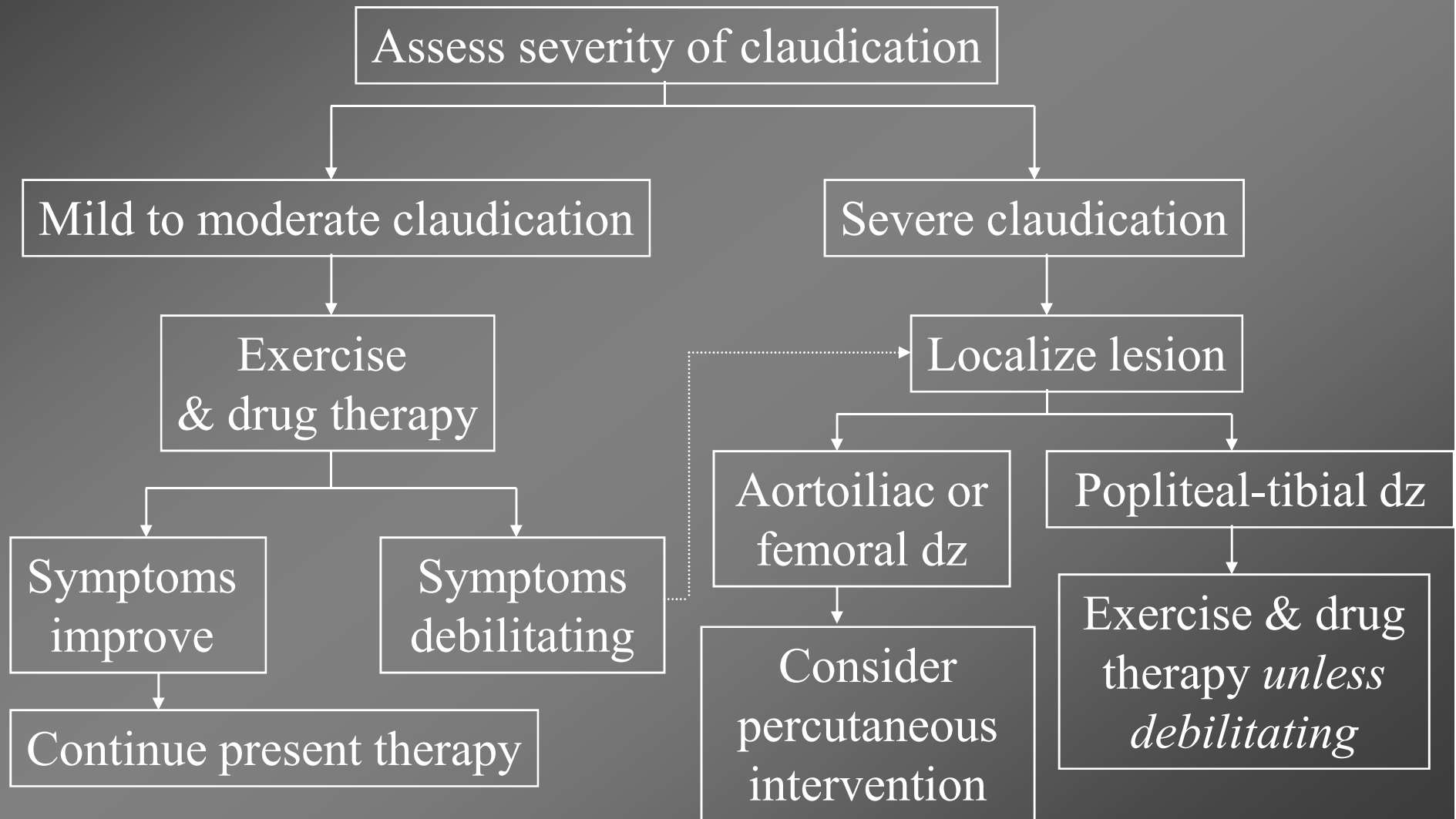
1 1151 1 1 1 1201 1 1 1

He has resolution of his left leg claudication.

ABI improved from 0.5 to 0.75.

He is now >3 year post intervention
and without claudication or cardiac events.

Treatment Approach to Intermittent Claudication



PAD Case #3

- A 66 year old male presents with intense rest discomfort of his left foot
- He was previously seen with claudication of both legs and placed on Pletal
- He has a history of HIV with peripheral neuropathy, dyslipidemia and tobacco use.
- Medications include pravastatin, Lopinivir/Rotinivir, Abacavir, Lamivudine, Nortriptyline, Gabapentin
- Exam reveals non-palpable pulses in left leg with pallor upon elevation and dependent rubor
- Labs with ABI 0.5 on left and 0.9 on right

Lower Extremity Segmental Pressures

	Right	Index	Left	Index
• Brachial	122 mmHg		123 mmHg	
• Thigh	127 mmHg	1.03	66 mmHg	0.54
• Calf	115 mmHg	0.93	64 mmHg	0.52
• Ankle/PT	108 mmHg	0.88	63 mmHg	0.51
• Ankle/DP	114 mmHg	0.93	57 mmHg	0.46

Lower Extremity Pulse Volume Recording

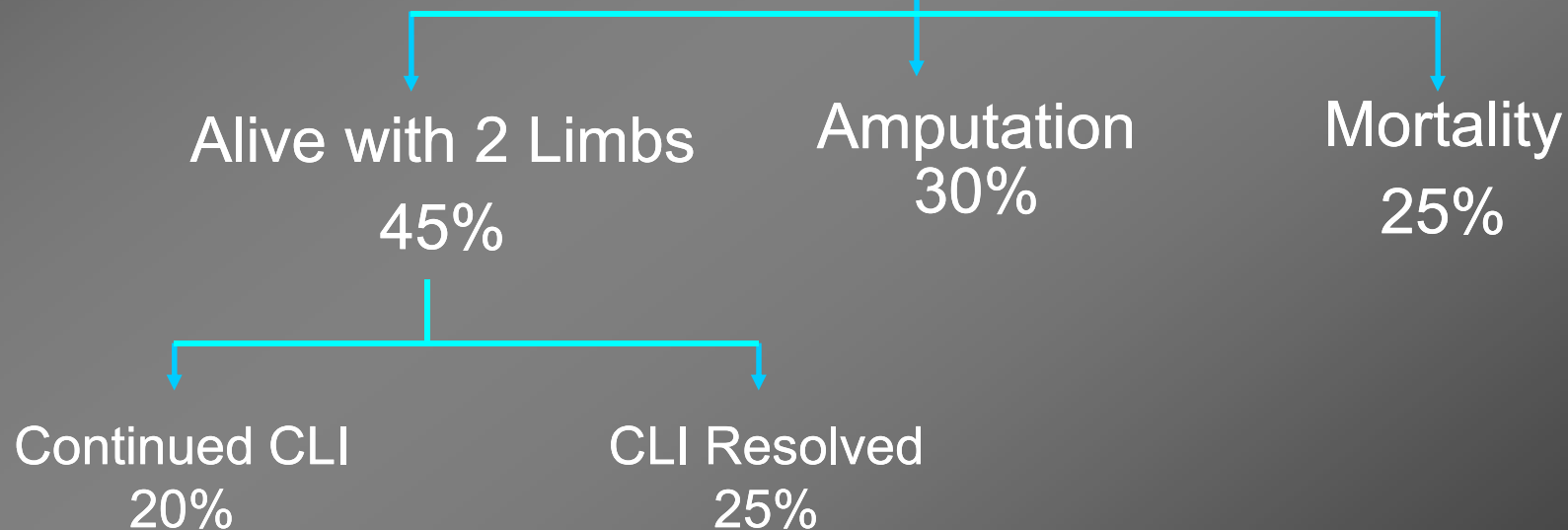
	Right	Amplitude	Left	Amplitude
• Thigh	Normal	16	Moderate	11
• Calf	Mild	17	Moderate	11
• Ankle	Normal	18	Moderate	9
• Metatarsal	Normal	15	Severe	

What should be done in his management?

Natural History of Critical Limb Ischemia

Critical Limb Ischemia
(*Rest Pain, Ulceration or Gangrene*)
1-3%

1-Year Outcomes

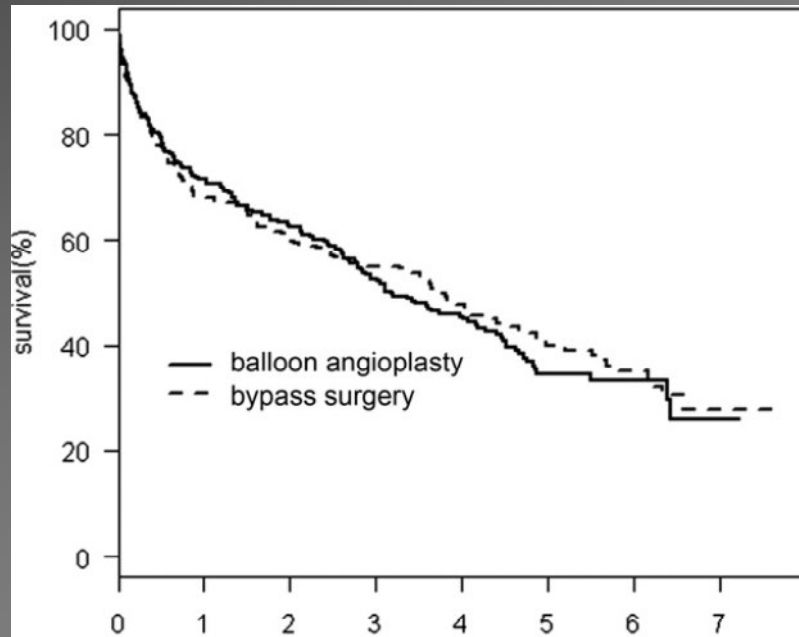


Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial

- Compared angioplasty first with surgery first for critical limb ischemia - 195/228 (86%) bypass surgery and 216/224 (96%) balloon angioplasty
- Compared with angioplasty, surgery was associated with
 - lower immediate failure (3% versus 20%)
 - higher 30-day morbidity (57% versus 41%)
 - lower 12-month reintervention (18% versus 26%)

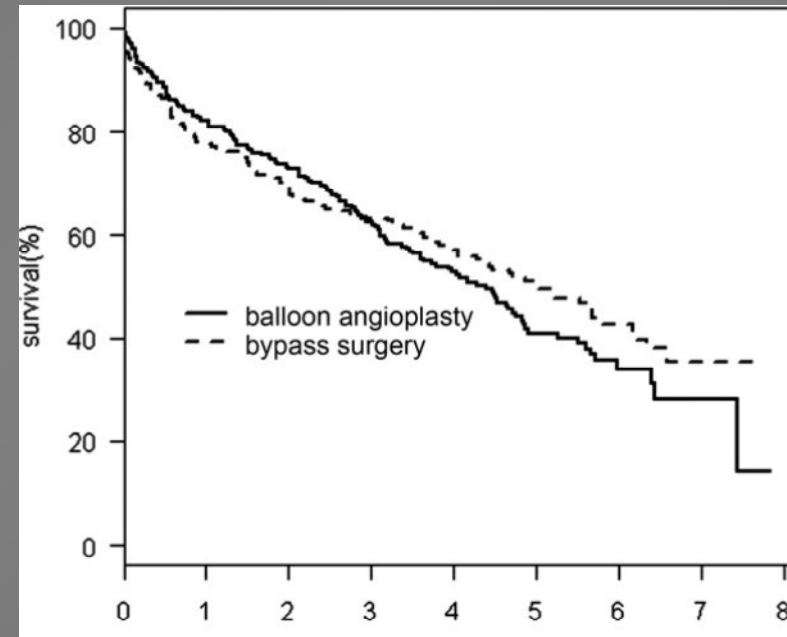
Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial

Amputation Free Survival



At risk	0	1	2	3	4	5	6	7
Balloon angioplasty	224	160	139	117	87	41	16	5
Bypass surgery	228	154	138	124	93	53	24	6

Overall Survival



At risk	0	1	2	3	4	5	6	7	8
Balloon angioplasty	224	184	162	139	101	49	19	7	
Bypass surgery	228	175	155	142	110	63	31	7	

Cox proportional hazards analysis for surgery first by time from randomization < 2 years and > 2 years

End point	Time	Estimate	95% CI	P-value
<i>Amputation-free survival</i>				
Unadjusted	Before 2 years	1.05	(0.78 to 1.41)	0.76
	After 2 years	0.80	(0.55 to 1.16)	0.24
Adjusted	Before 2 years	1.03	(0.76 to 1.39)	0.85
	After 2 years	0.85	(0.50 to 1.07)	0.11
<i>Overall survival</i>				
Unadjusted	Before 2 years	1.17	(0.83 to 1.65)	0.36
	After 2 years	0.62	(0.43 to 0.90)	0.01
Adjusted	Before 2 years	1.19	(0.84 to 1.68)	0.32
	After 2 years	0.61	(0.50 to 0.75)	0.009

* Adjusted for stratification, creatinine, body mass index, diabetes, age, smoking, statin at baseline and below-knee Bollinger angiogram score.

Recommendations for CLI: Endovascular and Open Surgical Treatment for Limb Salvage



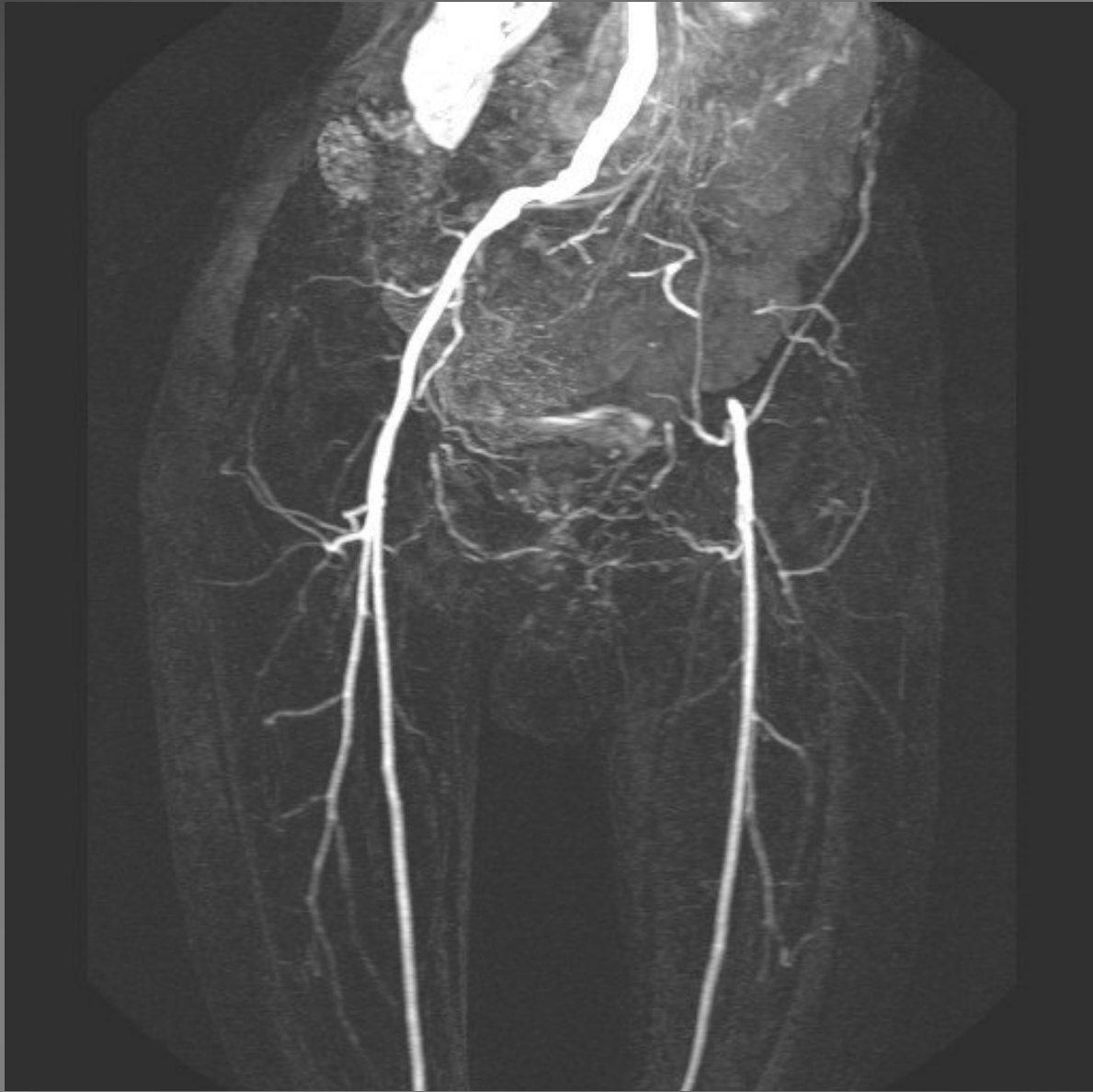
For patients with limb-threatening lower extremity ischemia and an estimated life expectancy of <2 years or in patients in whom an autogenous vein conduit is not available, balloon angioplasty is reasonable to perform when possible as the initial procedure to improve distal blood flow.



For patients with limb-threatening ischemia and an estimated life expectancy of >2 years, bypass surgery, when possible and when an autogenous vein conduit is available, is reasonable to perform as the initial treatment to improve distal blood flow.

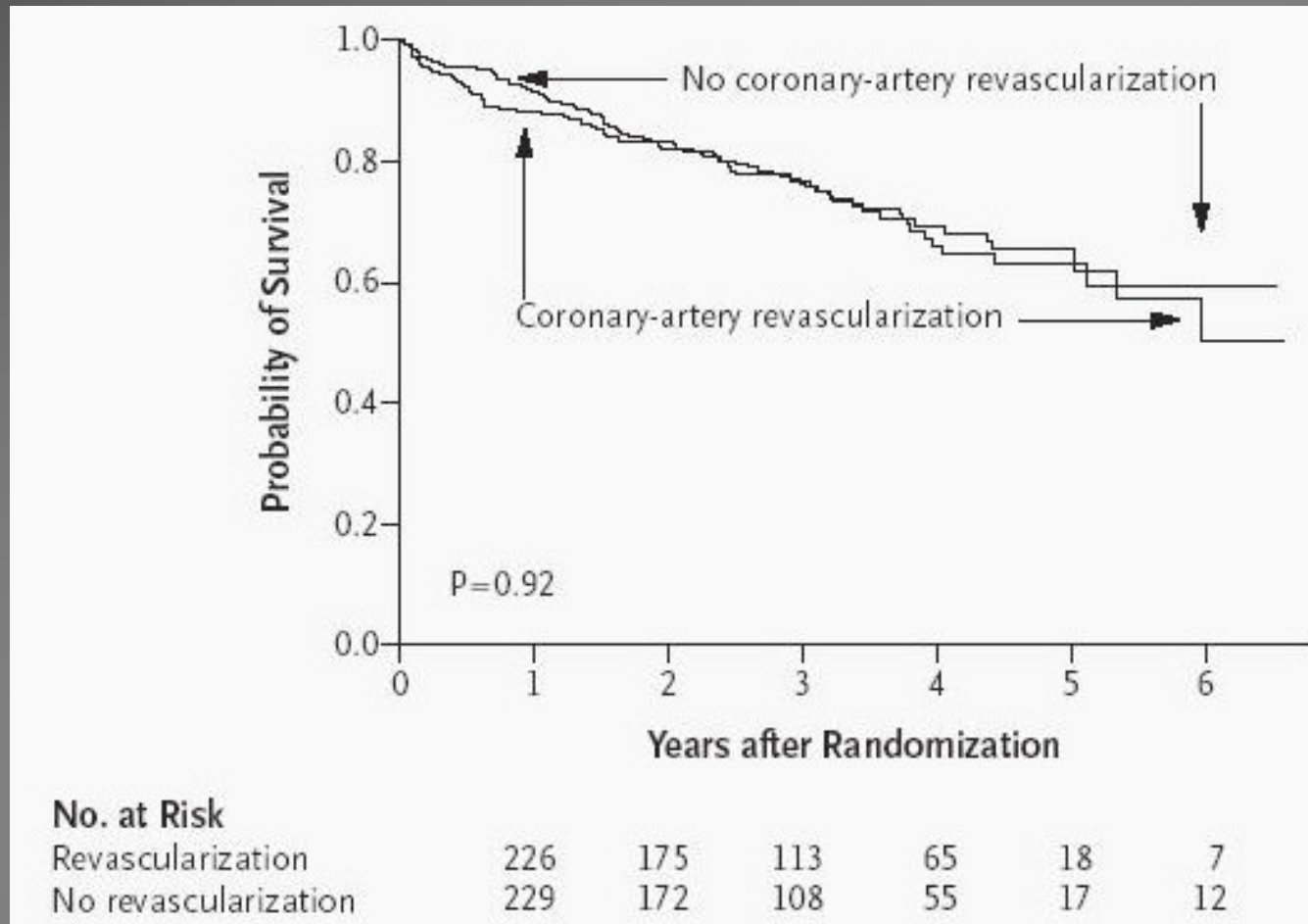
General Principle for Revascularization

- Claudicants should be revascularized only after a trial of exercise and pharmacotherapy.
 - An exception may be isolated iliac artery stenosis.
- Inflow and outflow should always be assessed prior to revascularization. Inflow lesions should be revascularized first followed by outflow lesions if bothersome symptoms persist.
- Revascularization for critical limb ischemia with associated tissue loss should aim to provide straight line flow to the foot.

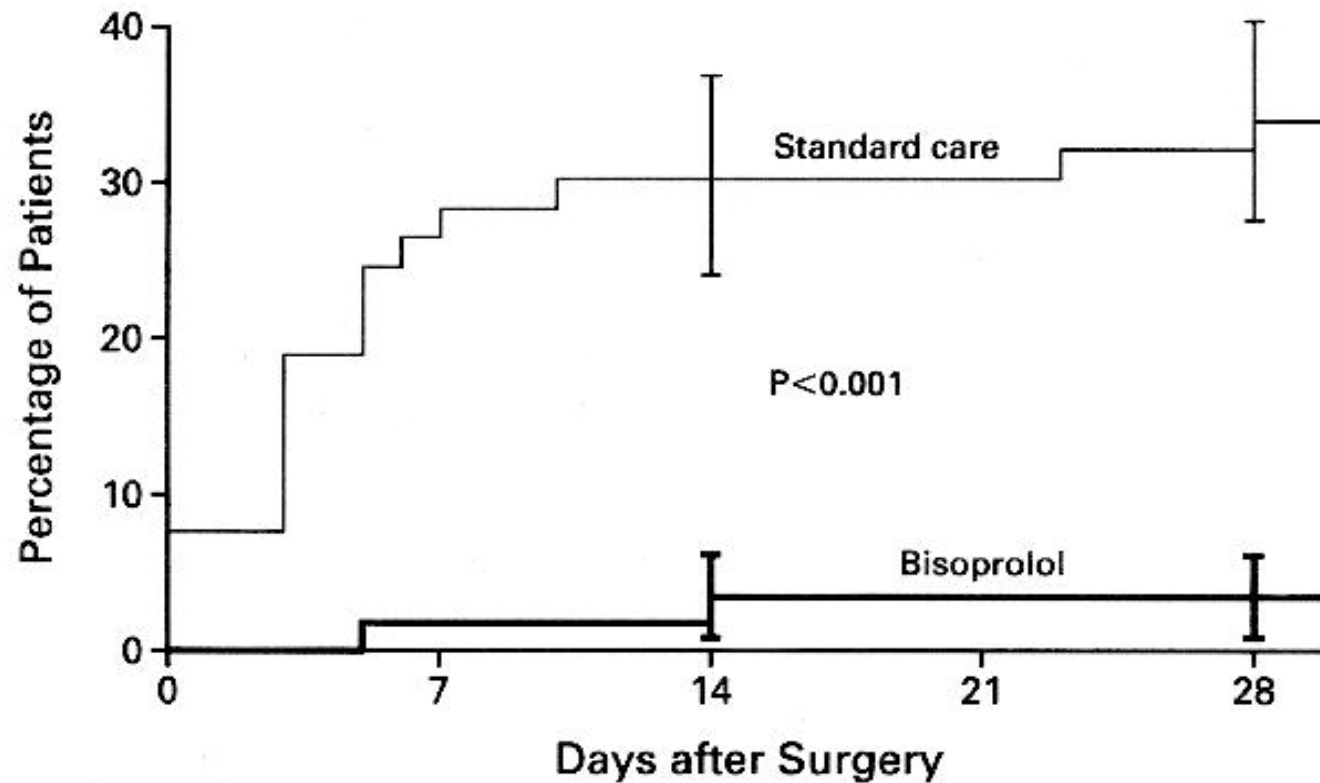


- The patient underwent angiography revealing a 70% R iliac artery stenosis and a long occlusion of the L iliac arteries
- Attempt to cross L iliac lesion was unsuccessful
- He underwent R iliac artery stent placement followed by a R to L femoral to femoral artery bypass graft
- Resolution of his rest ischemia to his left foot

Use of Coronary Revascularization Prior to Vascular Surgery



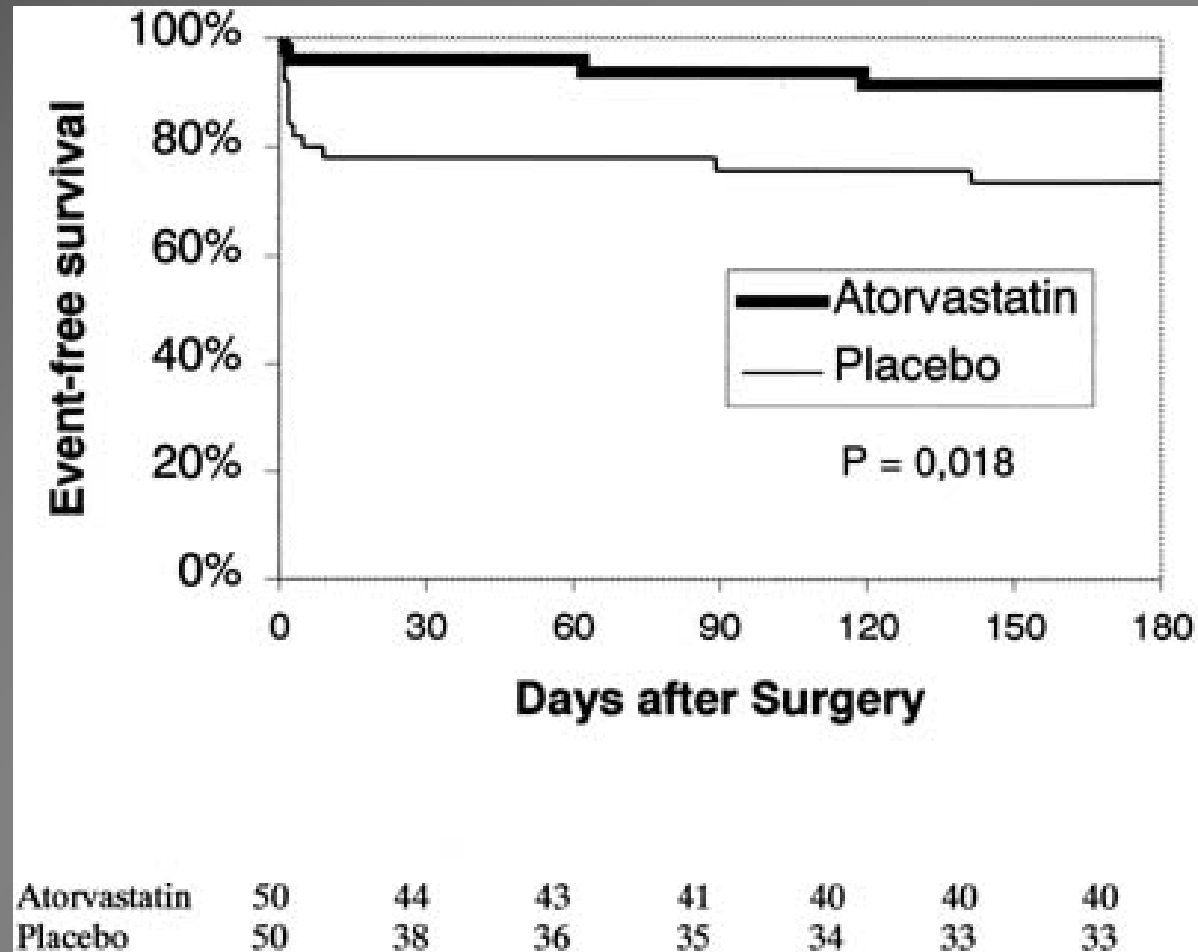
Use of Beta-Blockade during Vascular Surgery



No. AT RISK

Standard care	53	38	37	37	35
Bisoprolol	59	58	57	57	57

Use of Statin Therapy during Vascular Surgery



Summary of PAD and Its Management

- PAD is common and has a significant impact upon cardiovascular outcomes
- Treatment of PAD, even asymptomatic, should focus on risk factor modification/risk reduction
- Treatment of intermittent claudication should include exercise therapy, drug therapy and selective use of revascularization
- Treatment for critical limb ischemia warrants aggressive efforts at revascularization, including surgery, to reduce the risk of amputation