

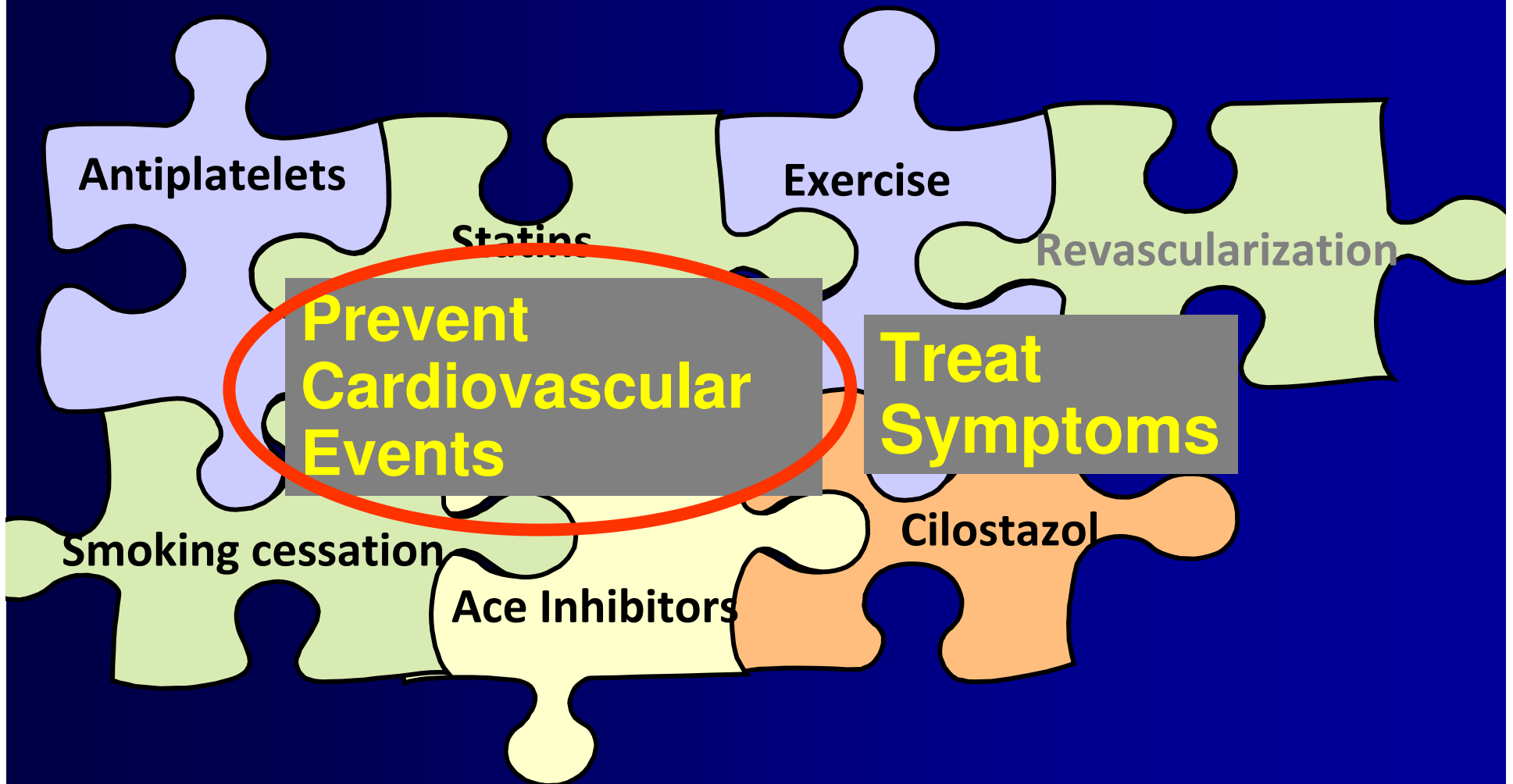
**Claudication:
Medical Therapy and Exercise**

Joshua A. Beckman, MD

Director, Cardiovascular Fellowship

Brigham and Women's Hospital

Therapies for Patients with PAD



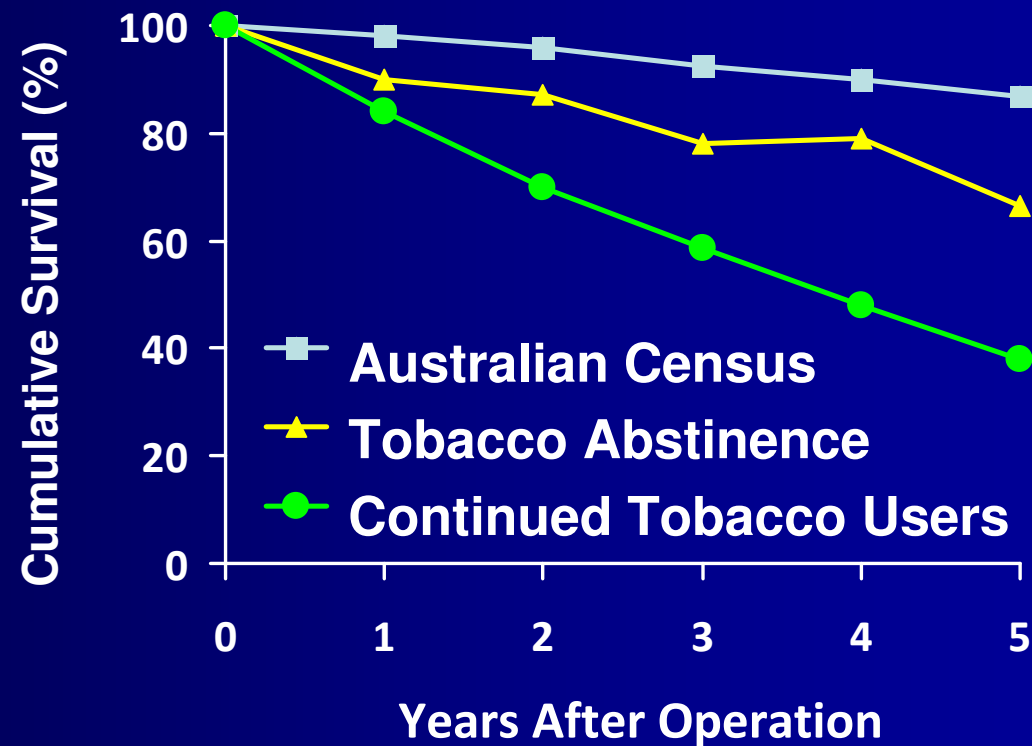
Reducing Cardiovascular Morbidity and Mortality in Patients with PAD

- Smoking cessation
- Cholesterol reduction
- Antihypertensive therapy [Aces and ARBs]
- Antiplatelet therapy

- Treatment of diabetes?
- Treat hyperhomocysteinemia

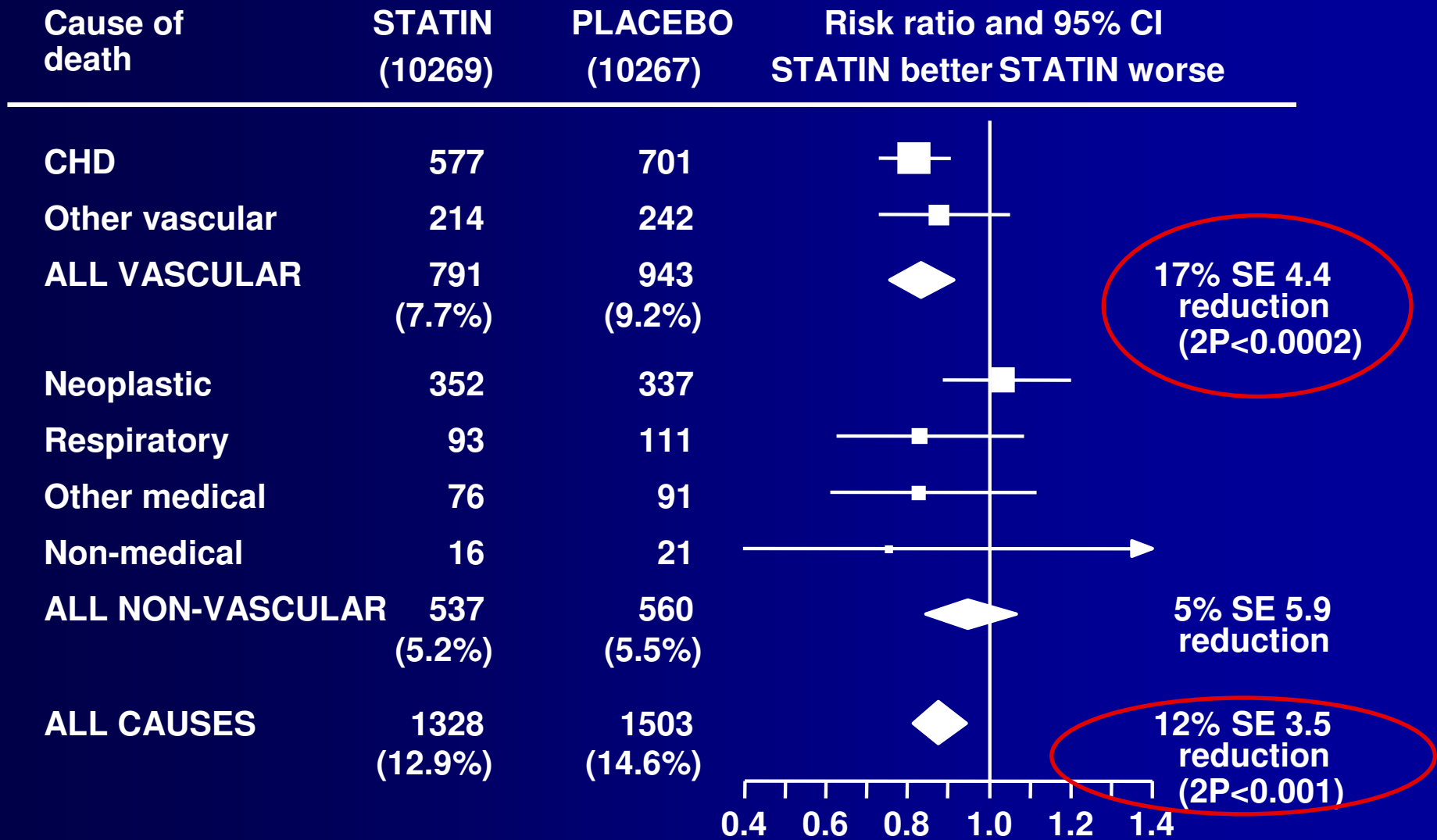
Effect of Smoking Cessation on Survival

N=133 After
Bypass Graft or
Lumbar
Sympathectomy
Surgery



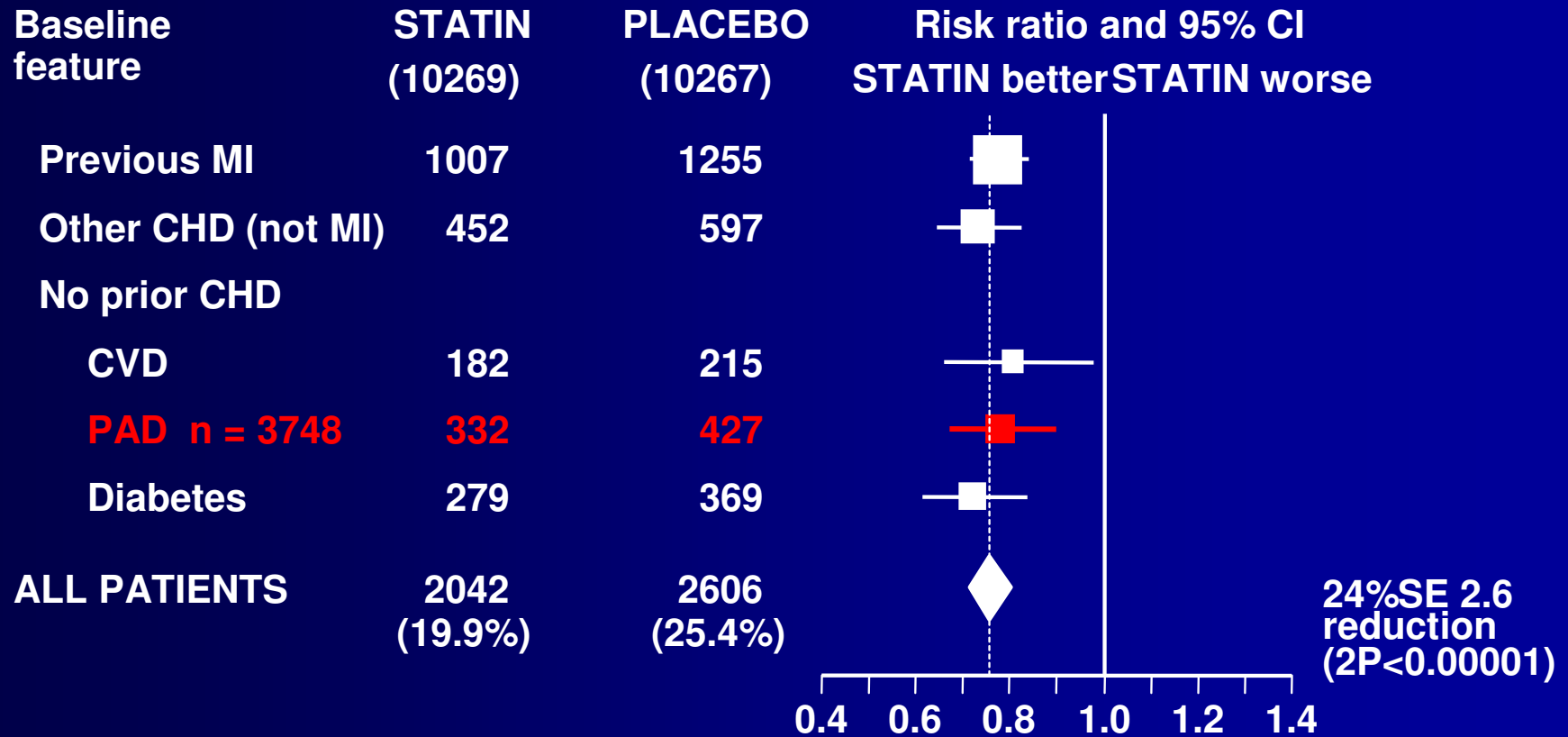
Faulkner KW. Med J Aust. 1983;1:217.

Statins: The Heart Protection Study



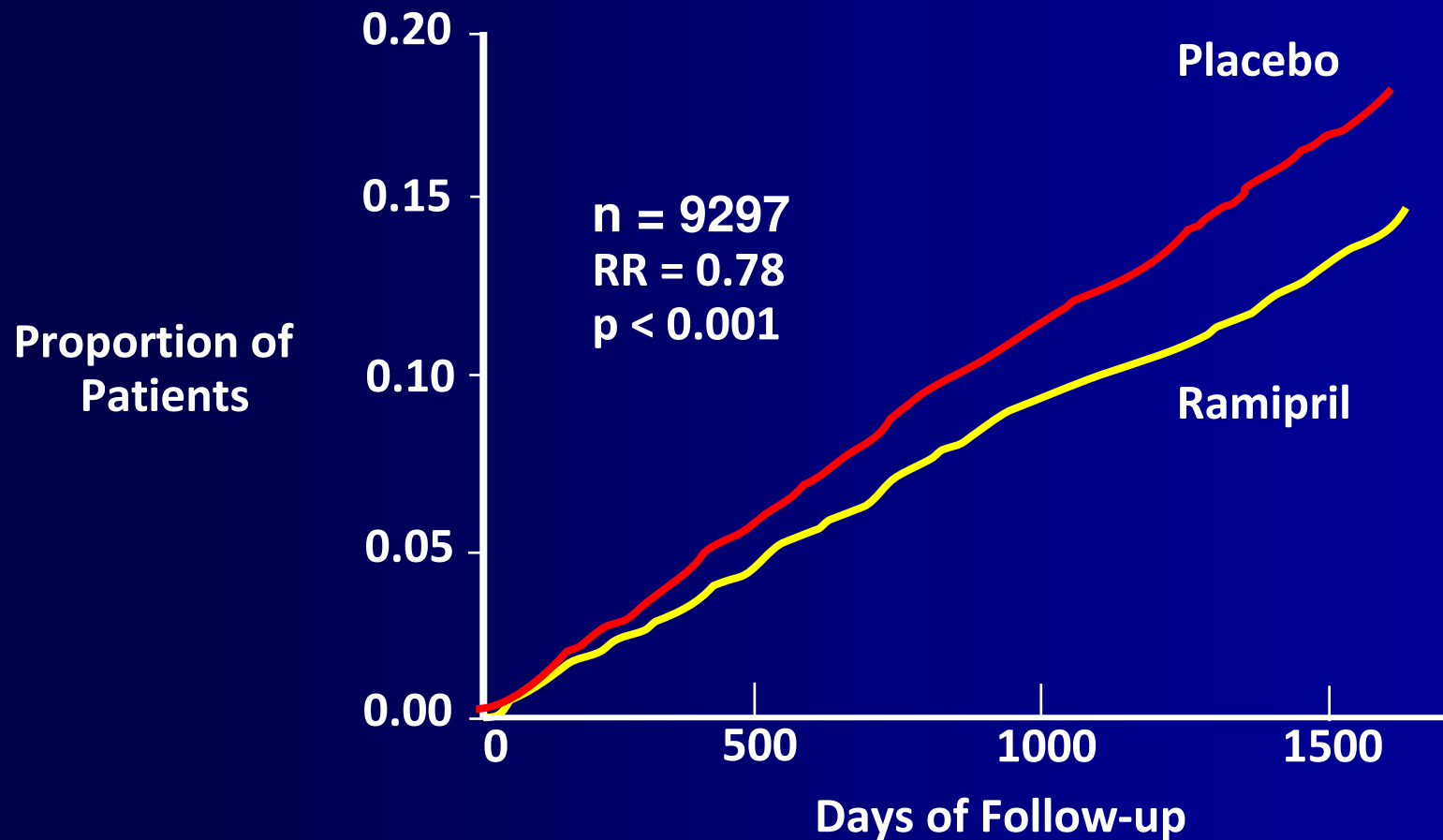
Heart Protection Study, Lancet, 2002

Heart Protection Study: Vascular Event by Prior Disease



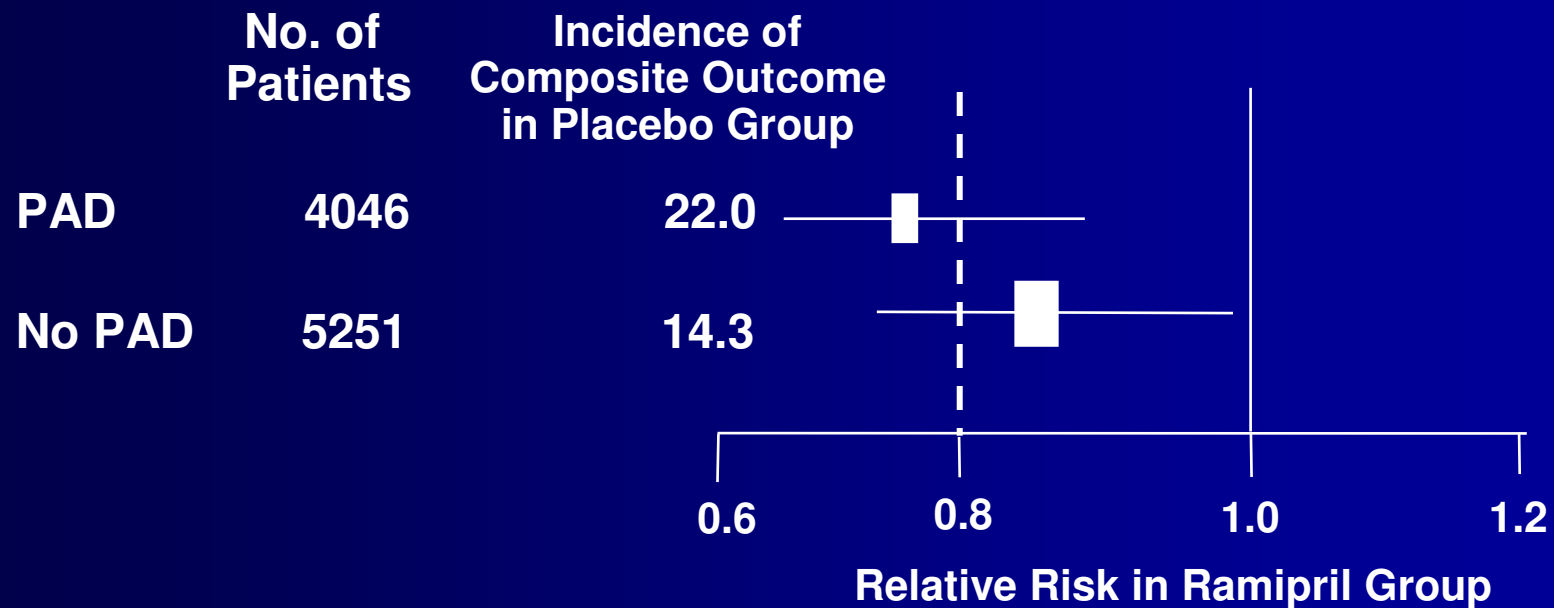
Heart Protection Study, Lancet, 2002

The HOPE Study: Effect of Ramipril on MI, Stroke or Cardiovascular Death

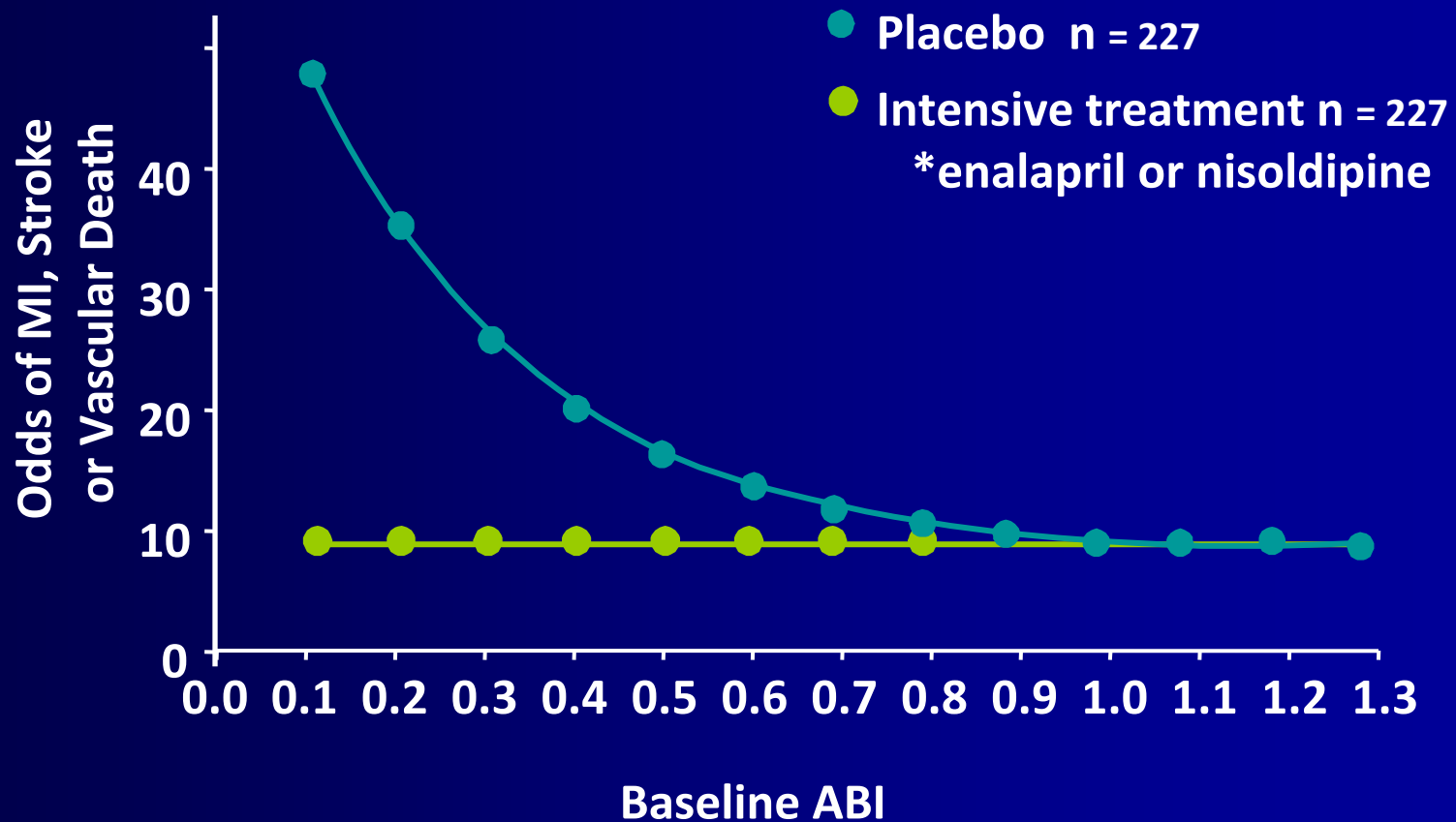


The HOPE Study Investigators N. Engl. J. Med. 2000; 342: 145-153

The HOPE Study: PAD Subgroup Analysis



Intensive BP Therapy in Diabetics with PAD: The ABCD Trial



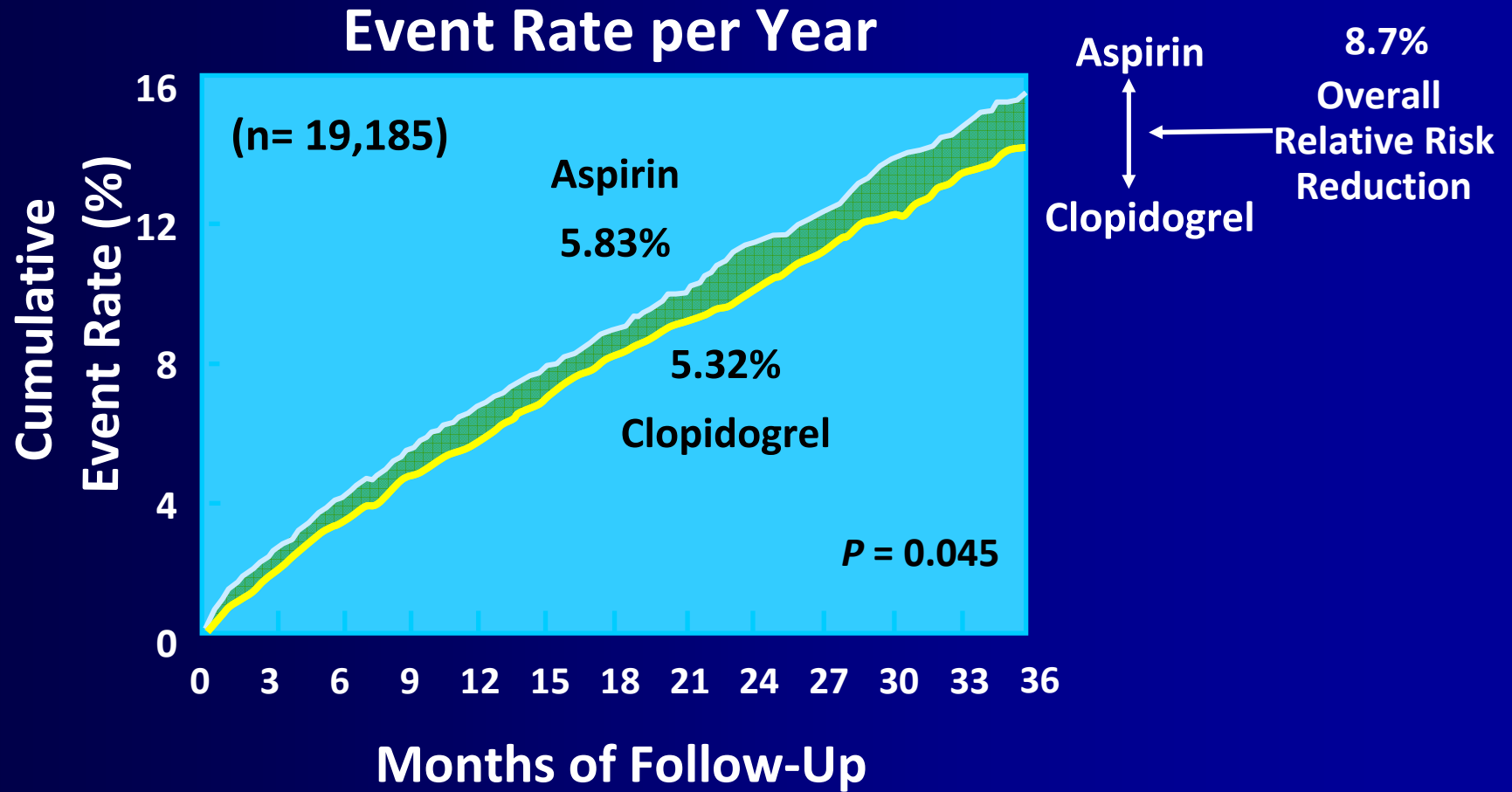
General Considerations for the Treatment of HTN in PAD

- **Blood pressure lowering is indicated to reduce the risk of stroke, MI, CHF, CRF, and death**
- **Intensive BP control especially important in diabetic patients**
- **B-blockers, Alpha-Blockers, vasodilators, and all other drug classes are acceptable.**
- **Only major reductions in perfusion pressure may worsen claudication**

Anti-thrombotic Trialists' Collaboration: PAD

- 42 clinical trials
- 9,214 patients with PAD
- 23% reduction in serious adverse vascular events ($P=.004$)
- Benefits similar among PAD subtypes (intermittent claudication, peripheral grafting, and peripheral angioplasty)

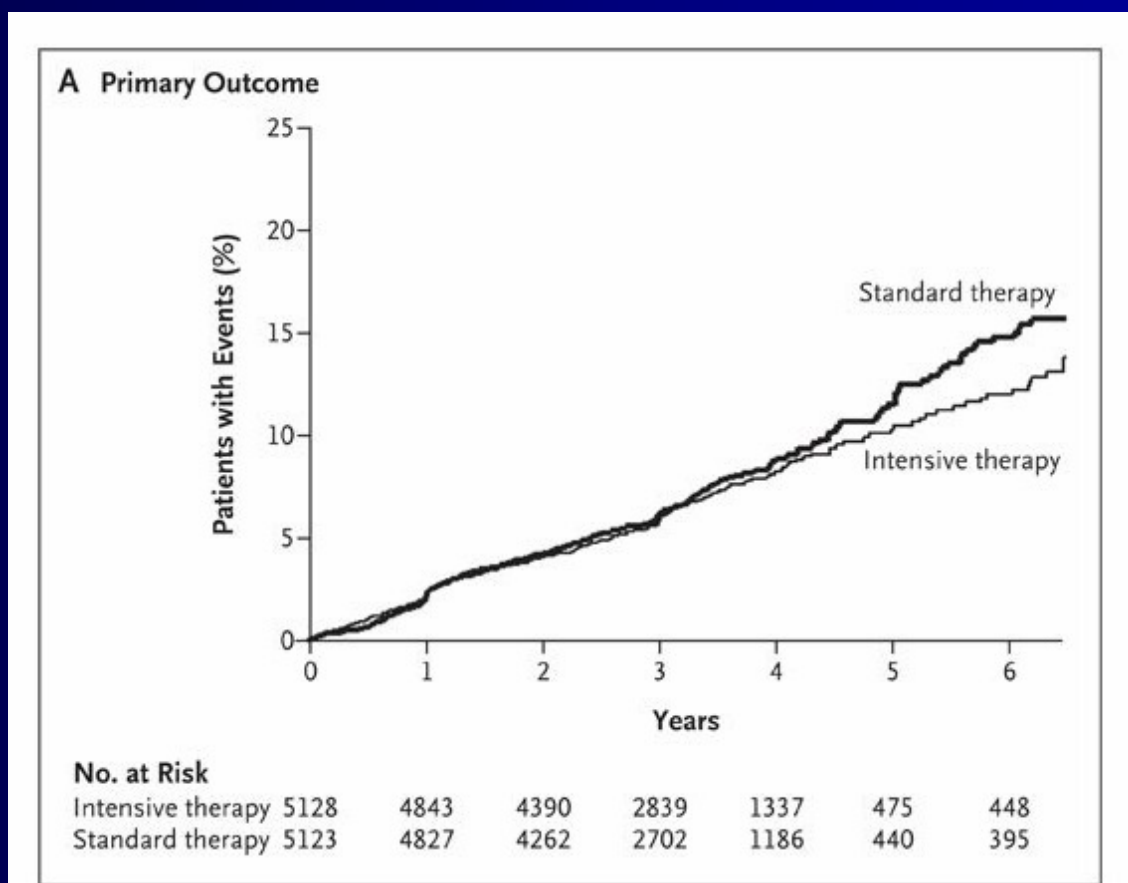
Efficacy of Clopidogrel vs. Aspirin in MI, Ischemic Stroke, or Vascular Death



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

Effects of Intensive Glucose Lowering in Type 2 Diabetes: *ACCORD*

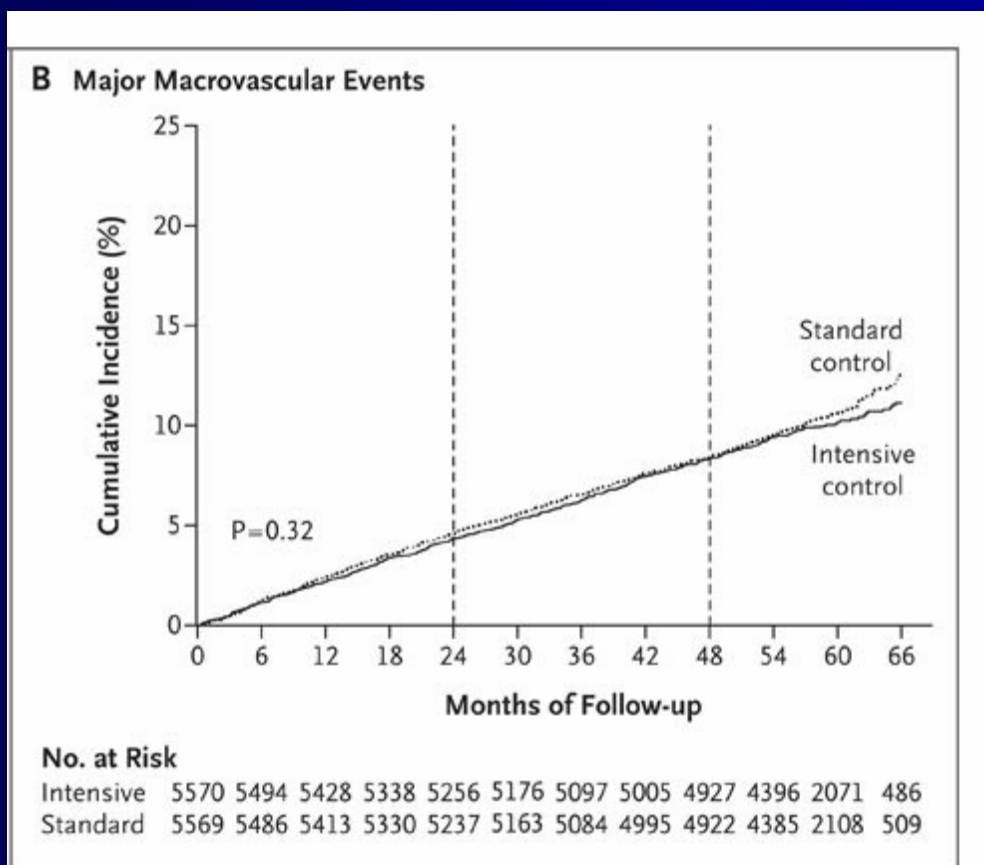
10,251 patients (mean age, 62.2 yrs) with a median Hgb A1c level of 8.1% randomized to intensive therapy (Hgb A1c 6.4%) or standard therapy (Hgb A1c 7.5%)



ACCORD Study Group NEJM 2008;358:2545

Effects of Intensive Glucose Lowering in Type 2 Diabetes: *ADVANCE*

11,140 patients with type 2 DM randomized to standard glucose control (Hgb A1c 7.3%) or intensive glucose control (Hgb A1c 6.5%)

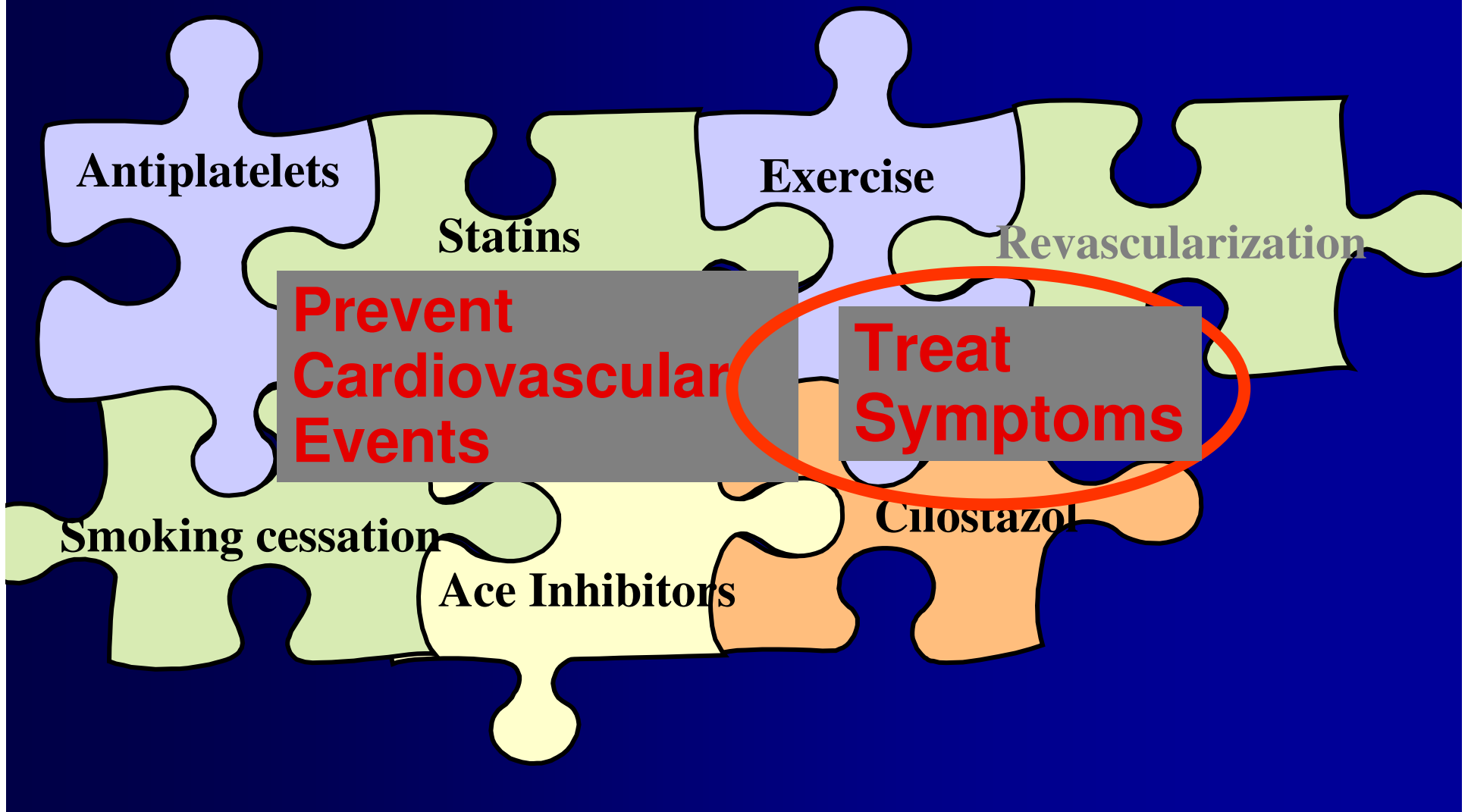


ADVANCE Study Group NEJM 2008;358:2560

Glycemic Control in Diabetic PAD Patients

- **Dramatically reduces incidence of microvascular events**
 - Type I (DCCT), Type II (UKPDS)
- **No reductions for type 2 subjects in large clinical trials**
 - UKPDS
 - ACCORD, ADVANCE, VADT
- **Insulin-sensitizing agents may reduce incidence of macrovascular complications**
 - UKPDS 34 - metformin in obese diabetics
 - Thiazolidinediones (VA study ongoing)
- **Treat all diabetics to goal HgB A1C < 7% to prevent *microvascular events***

Therapies for Patients with PAD



Treatment of Intermittent Claudication

- Supportive Care
 - Foot care and foot self-inspection
- Walk!
Exercise rehabilitation
- Pharmacotherapy
- Consider Revascularization

Claudication Exercise Programs

- Supervised 3 times/week, 2 times unsupervised
- Duration: 3 to 6 months
- Effective at improving exercise performance, walking ability and physical functioning
- Safe
- Cost-effective
- Not reimbursed by most payors!

Efficacy of Supervised Exercise for Claudication

21 Study Meta Analysis

	<u>Exercise</u>	<u>Control</u>	<u>Change</u>	<u># Blocks</u>
• ICD Blocks	180%	40%		2
• ACD Blocks	130%	30%		3
• Predictors of Response:				
– Walking exercise				1 block = 80 meters
– Walking to near-maximal pain				
– >6 months				
– Supervised				
– Sessions > 30 minutes and at least 3 x per week				

Pharmacotherapy for PAD

FDA Approved Drugs

- Pentoxifylline
- **Cilostazol**

Drugs Under Investigation

- Atorvastatin
- Rosiglitazone
- Propionyl- L-Carnitine
- L-Arginine
- Prostaglandins
- Angiogenic Factors

VEGF

bFGF



Cilostazol (Pletal)

Drug Class Phosphodiesterase III inhibitor derivative
(↑cAMP)

Approved January 1999

Dosing

Pharmacologic

Properties

**? Mechanism of
Action in Rx of
Claudication**

inhibitor

Prevents arterial thrombi

Vasodilation

↑ ABI

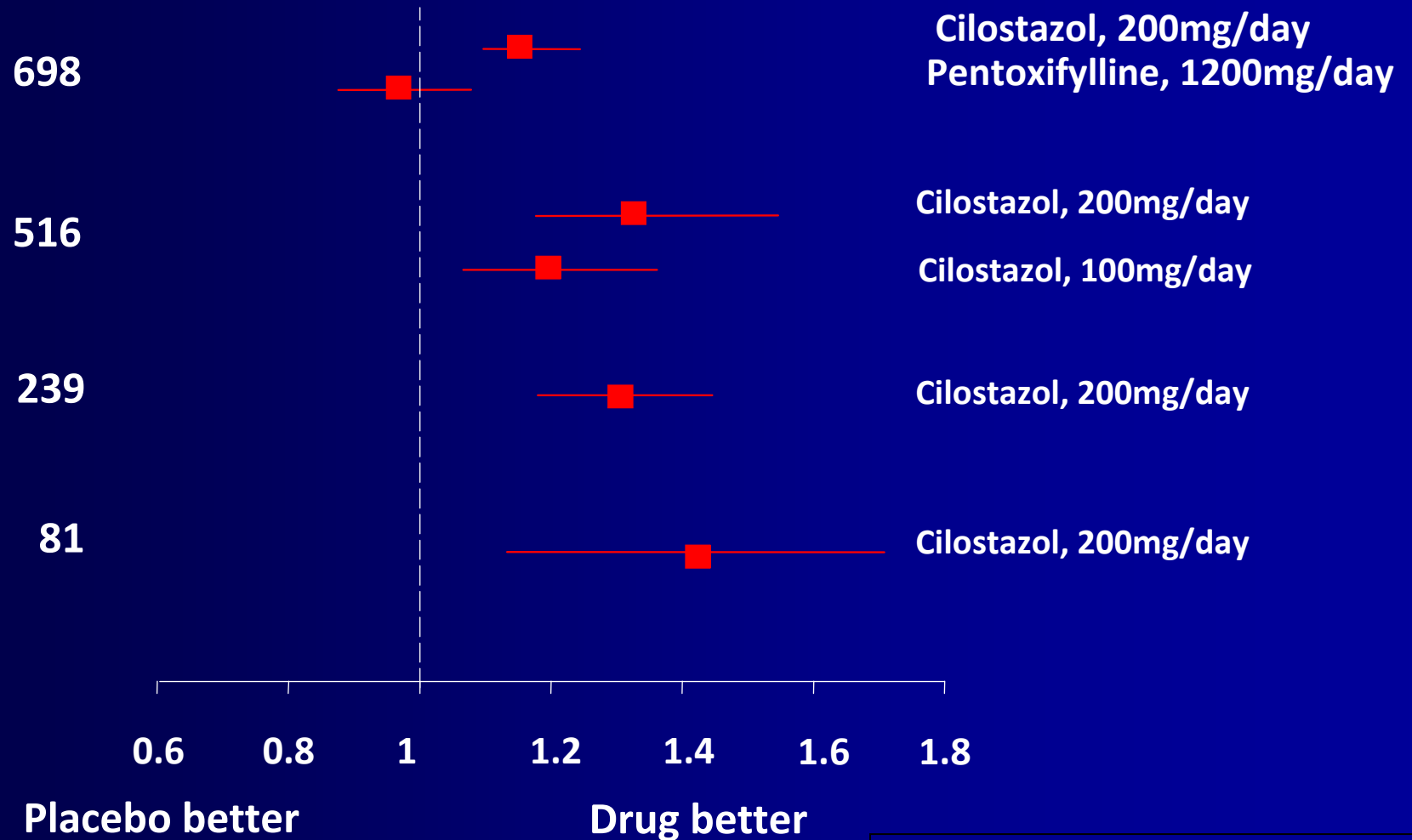
↑ HDL-cholesterol (10%)

↓ Triglycerides (15%)

Inhibits smooth muscle cell proliferation *in vitro*

Effect of Cilostazol on Walking Distance in Patients with Intermittent Claudication

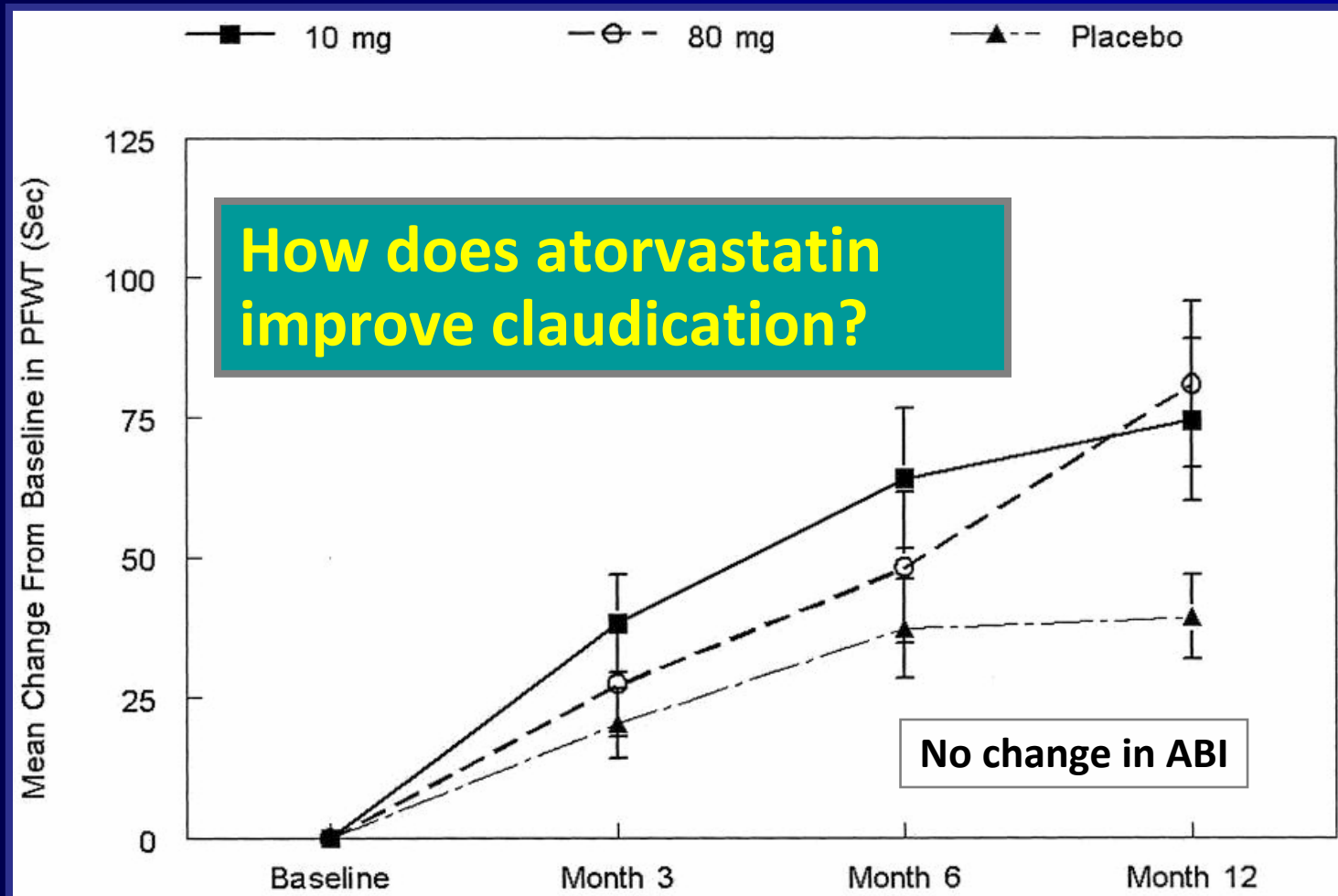
No. of Patients



Cilostazol Caveats and Cautions

- **BLACK BOX WARNING:** Pletal is contraindicated in patients with congestive heart failure of any severity
- Extensive CYP 3A4 Metabolism
 - Consider 50 mg BID dose
- Side effects common
 - Abnormal stools (15-20%)
 - Palpitations (~15%)
 - Headaches (~25%)

High Dose Atorvastatin Improves Pain-Free Walking Time in Patients with Claudication



Summary

- **Claudication is associated with significant morbidity and mortality**
- **Well-proved strategies can reduce both**
- **These therapies should be applied in all patients with claudication**