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Outcomes in Peripheral Artery Disease

CPC Clinical Research

PAD Outcomes

- **Outcomes can be grouped into**
- **Cardiovascular (Major Adverse Cardiovascular Events – MACE)**
 - Myocardial infarction
 - Stroke
 - Death
- **Limb (Major Adverse Limb Events – MALE)**
 - Revascularization
 - Major amputation
 - Acute limb ischemia

Ankle Brachial Index

- Used to diagnose and Stratify PAD
- The highest systolic pressure at the ankle (posterior tibial and dorsalis pedis arteries)
- Brachial pressure (typically same on each side but if not the highest)
- Divide the Highest ankle pressure/highest brachial pressure
- Values below 0.9 diagnostic of PAD (above 1.2 indicate calcified arteries and could be PAD)

- Example – patient has:
 - Posterior tibial pressure of 70.
 - Dorsalis pedis pressure of 80
 - Brachial pressure of 120
- **ABI equals 80/120 or 0.67**

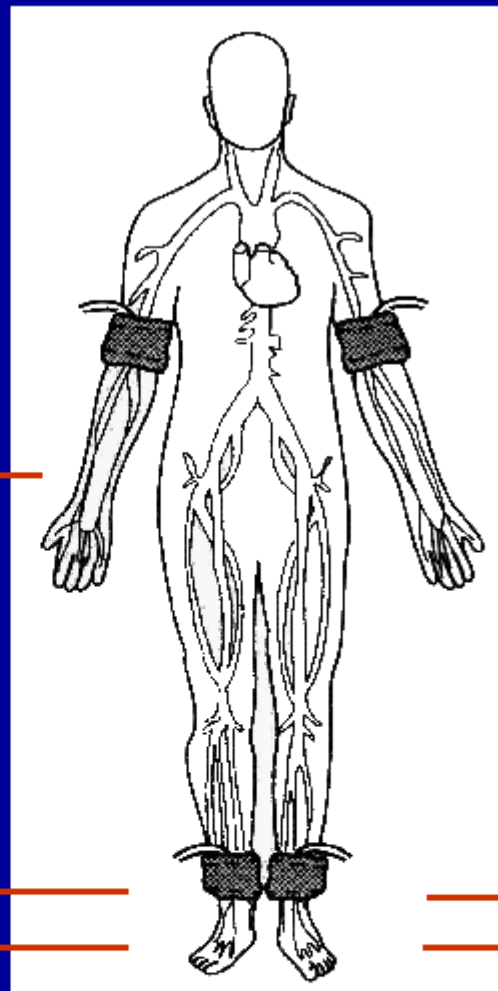
How to Perform and Calculate the ABI

PARTNERS Program ABI Interpretation

Above 0.90 — Normal
 0.71-0.90 — Mild Obstruction
 0.41-0.70 — Moderate Obstruction
 0.00-0.40 — Severe Obstruction

Right Arm Pressure:

Left Arm Pressure:



Pressure:

Pressure:

PT

PT

DP

DP

Right ABI

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

Left ABI

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

Example

$$\frac{\text{Higher Ankle Pressure}}{\text{Higher Brachial Pressure}} = \frac{92 \text{ mm Hg}}{164 \text{ mm Hg}} = 0.56$$

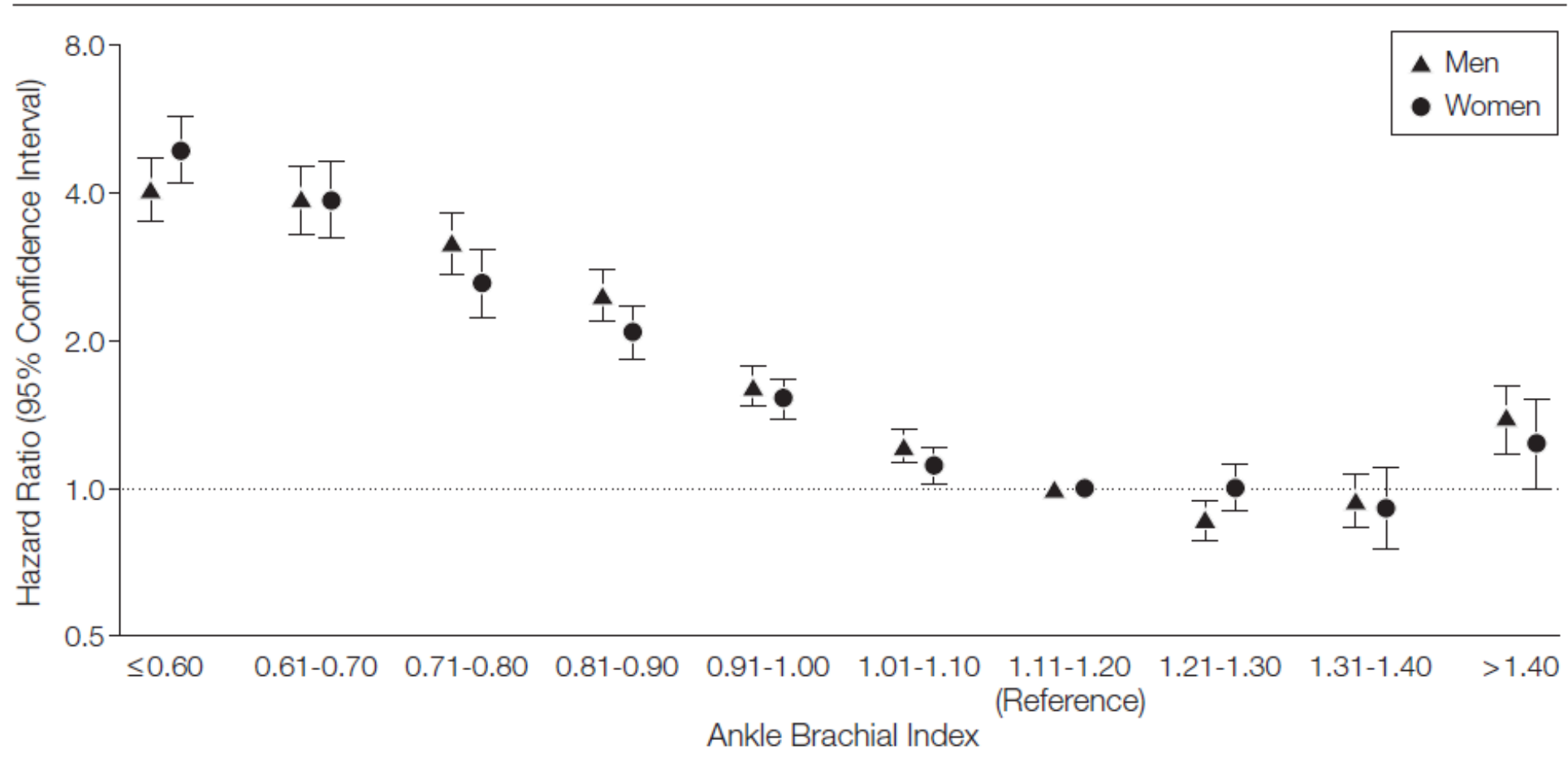
See ABI Chart

PAD Outcomes

- **PAD Mortality can be stratified by presenting PAD severity**
- **Severity is determined by the ankle brachial index (ABI)**
 - Lower values more severe
 - Values beyond 1.2 also consider severe due to calcification
- **This creates a mortality risk curve with elevations at both ends of the spectrum**

Total Mortality Hazard Ratios

Figure 2. Hazard Ratios for Total Mortality in Men and Women by Ankle Brachial Index at Baseline for All Studies Combined in the ABI Collaboration

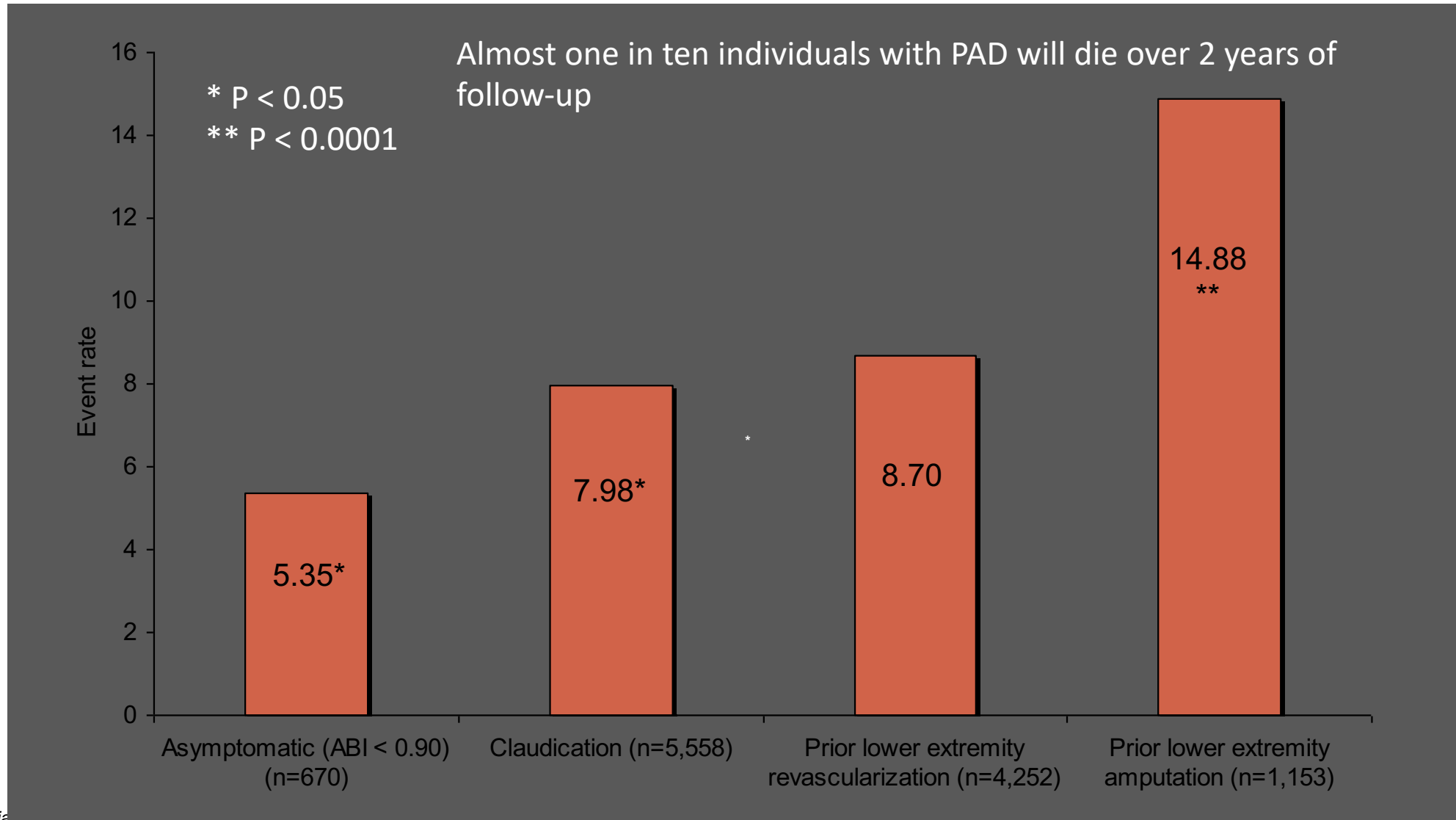


Hazard ratios are not adjusted for age or cardiovascular risk factors.

PAD Outcomes

- **PAD Mortality can also be stratified by presenting PAD severity based on PAD history**
- **Stratified by least to greatest:**
 - **Asymptomatic**
 - **Claudication**
 - **Prior lower extremity revascularization**
 - **Prior lower extremity amputation**

PAD Mortality over time based on severity of PAD symptoms – REACH Registry



Spectrum of Outcomes in PAD

Limb Ischemic Events Occur in a Spectrum Similar to Cardiac Ischemic Events

CARDIAC	Stable Angina	Elective Coronary Revasc.	Severe Stable Angina	Unstable Angina	Urgent Coronary Revasc.	Myocardial Infarction	Cardiovascular Death	
LIMB	Claudication	Elective Peripheral Revasc.	Chronic Critical Limb Ischemia Rest Pain	Chronic Critical Limb Ischemia Tissue loss	Urgent Peripheral Revasc.	Acute Limb Ischemia	Cardiovascular Death	
DEFINITION	Subjective						Objective	
REASON FOR INTERVENTION	Symptom Relief						Prevent Irreversible Tissue Loss	
ETIOLOGY	Multifactorial/Atherosclerotic						Thrombosis (artery, stent, graft)	

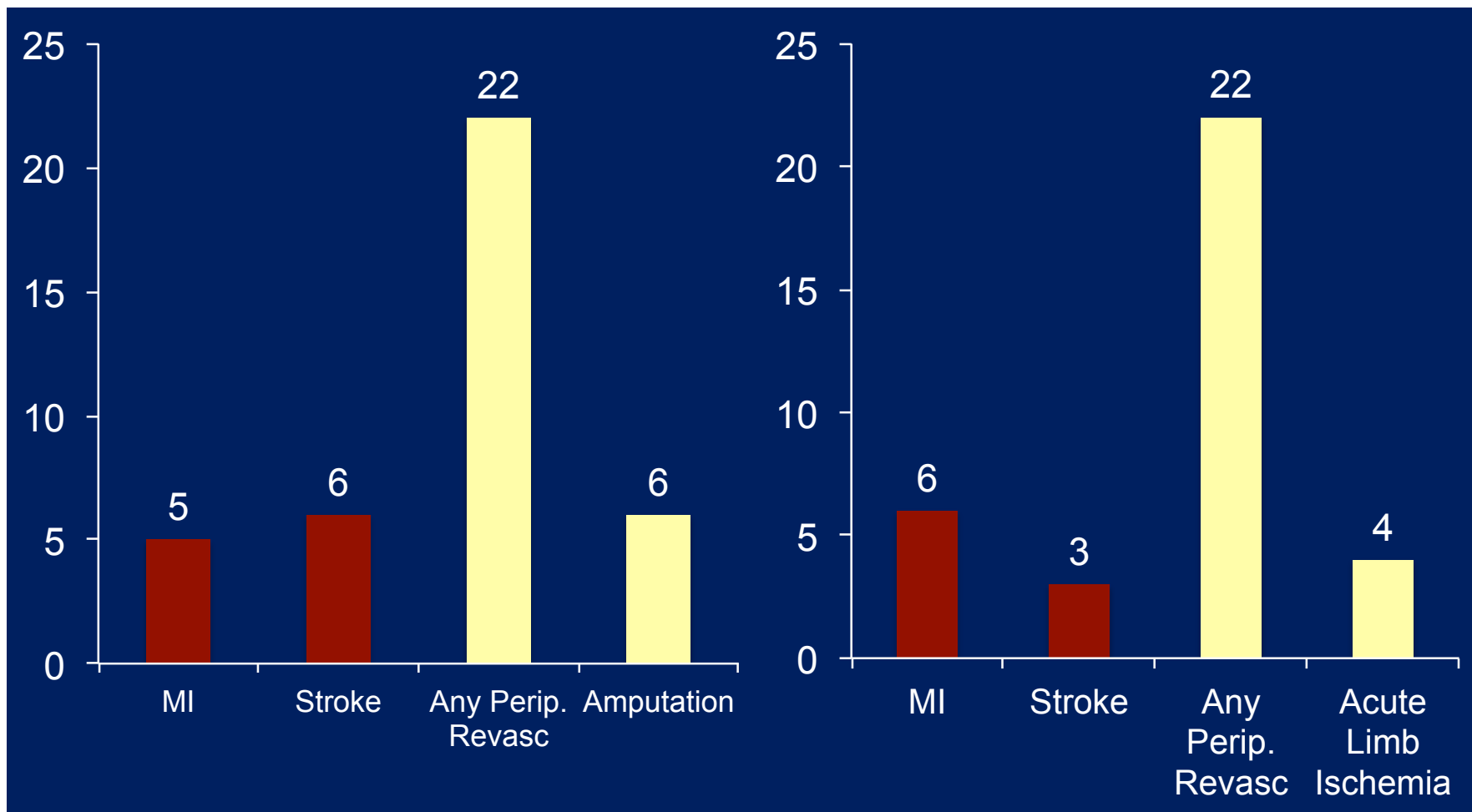
PAD Outcomes

- **Contributions of MACE and MALE outside of CV Death**
- **Examining events over time in:**
 - **PAD subgroup of large cardiovascular registry (Reduction in Atherosclerosis for Continued Health – REACH)**
 - **PAD subgroup of large cardiovascular clinical trial of antiplatelet therapy (Vorapaxar) TRA2°P-TIMI 50**

Burden of Risk in PAD is Driven by MALE more than MACE

Events in PAD Patients at 4 Years
REACH Registry

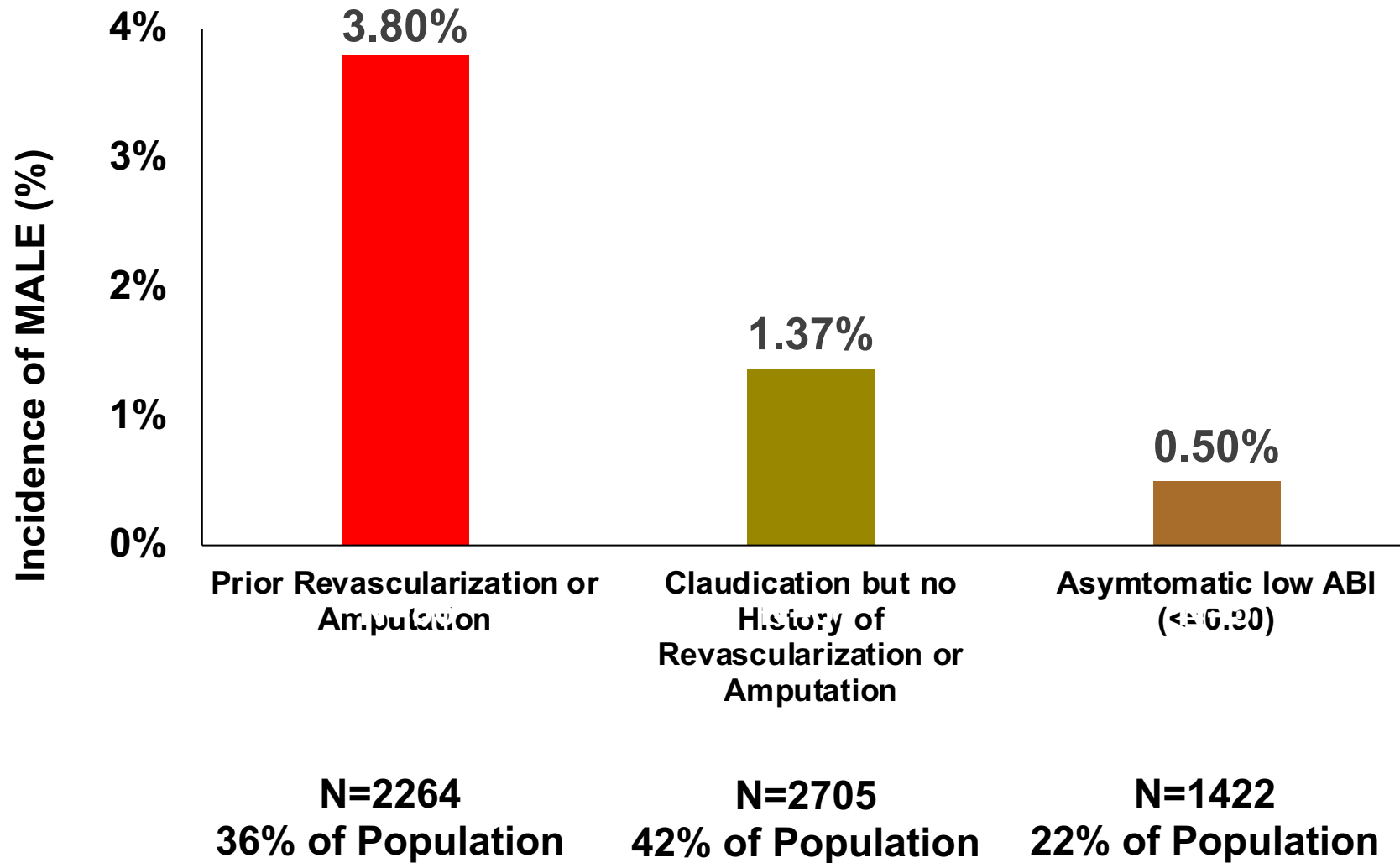
Events in PAD Patients at 3 Years
TRA2P-TIMI 50



PAD MALE Risk – Prior Revascularization

- **Prior Revascularization increases MALE risk in PAD**
- **Two large cardiovascular Trials**
- **COMPASS**
 - Randomized trial of low dose Rivaroxaban and aspirin in cardiovascular population (with PAD subgroup)
- **EUCLID**
 - Randomized trial of Ticagrelor vs clopidogrel in PAD population

Prior Limb Revascularization Associated with Greater Limb Risk – COMPASS Trial



Anand SS et al. JACC 2018;71:2306-15.

Prior Revasc also a major risk factor for ALI in EUCLID

Table 3. Baseline Factors Associated With ALI Hospitalization Among the Overall Study Population

	HR (95% CI)	P Value
Age, per 10 y	0.8 (0.7, 1.0)	0.02
BMI, per unit increase, kg/m ²	1.0 (0.7–1.0)	0.03
Region (South America as the reference)		0.03
Asia	1.1 (0.5–2.1)	0.88
Europe	1.8 (1.0–3.2)	0.04
North America	1.7 (0.9–3.2)	0.08
Previous lower extremity revascularization	4.7 (3.3–6.8)	<.01
Previous atrial fibrillation	1.8 (1.1, 3.2)	0.03
Baseline ABI		<.01
Per 0.1 ABI decrease in patients with baseline ABI ≤0.60	1.3 (1.1–1.5)	<.01
Per 0.1 ABI decrease in patients with baseline ABI >0.60	1.1 (1.0–1.2)	0.16
Baseline statin use	0.7 (0.5–0.9)	<.01
Baseline angiotensin receptor blocker use	0.7 (0.5–1.0)	0.05
Randomized treatment: ticagrelor (clopidogrel as reference)	1.0 (0.8–1.3)	0.91

ABI indicates ankle-brachial index; BMI, body mass index; CI, confidence interval; and HR, hazard ratio.

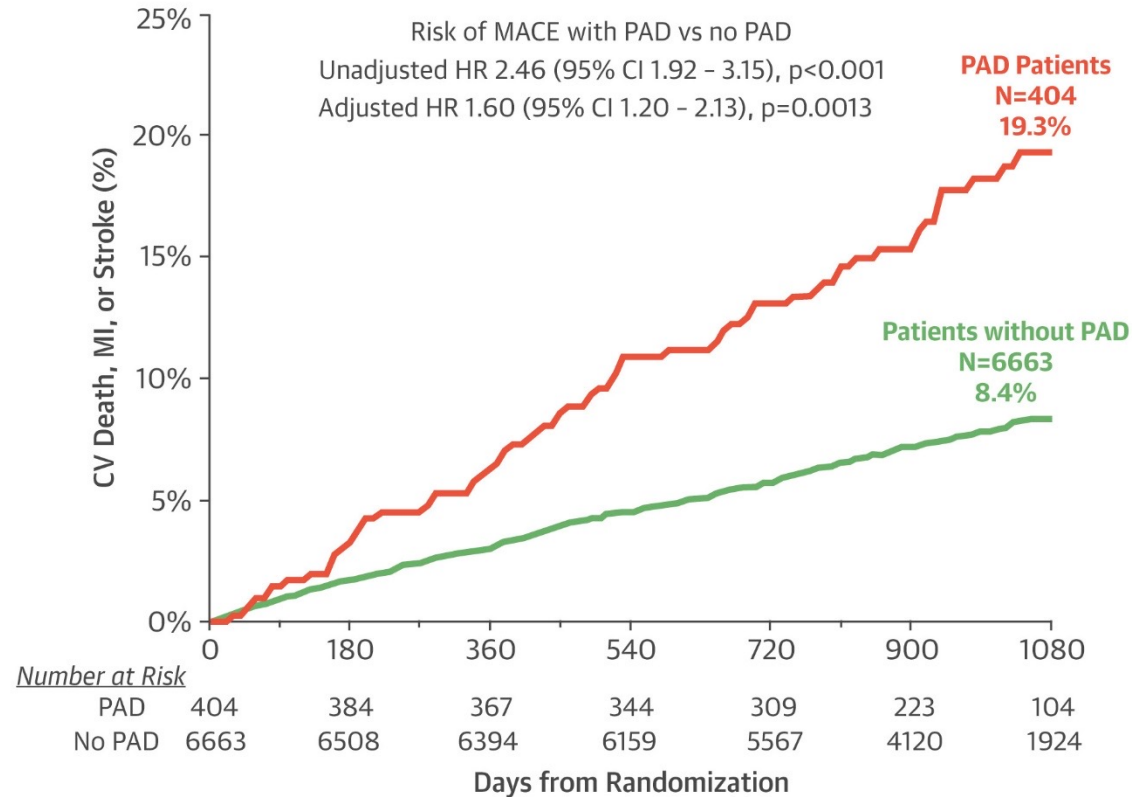
PAD increases MACE in high-risk populations

- **Pegasus – A large multicenter cardiovascular trial of ticagrelor and aspirin vs aspirin after myocardial infarction**
- **A population at higher risk for additional MACE**
- **Examining MACE in patients with and without baseline PAD is instructive**

PAD Increases Risk of MACE After MI

The risk of major cardiovascular (CV) events and major adverse limb events in patients with PAD and a prior MI in PEGASUS

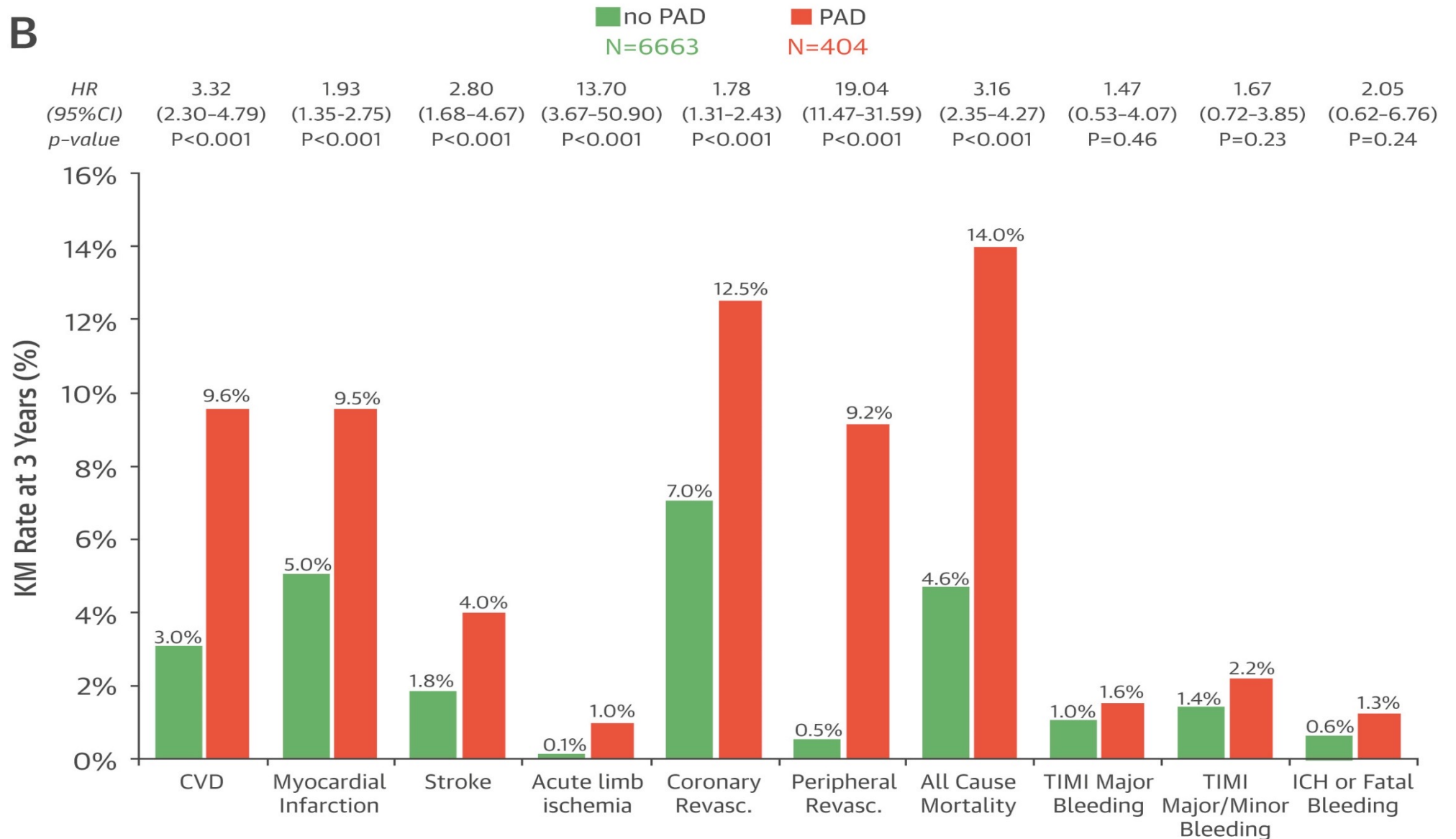
A



PAD Increases Risk of MACE/MALE After MI

The risk of major cardiovascular (CV) events and major adverse limb events in patients with PAD and a prior MI in PEGASUS

B



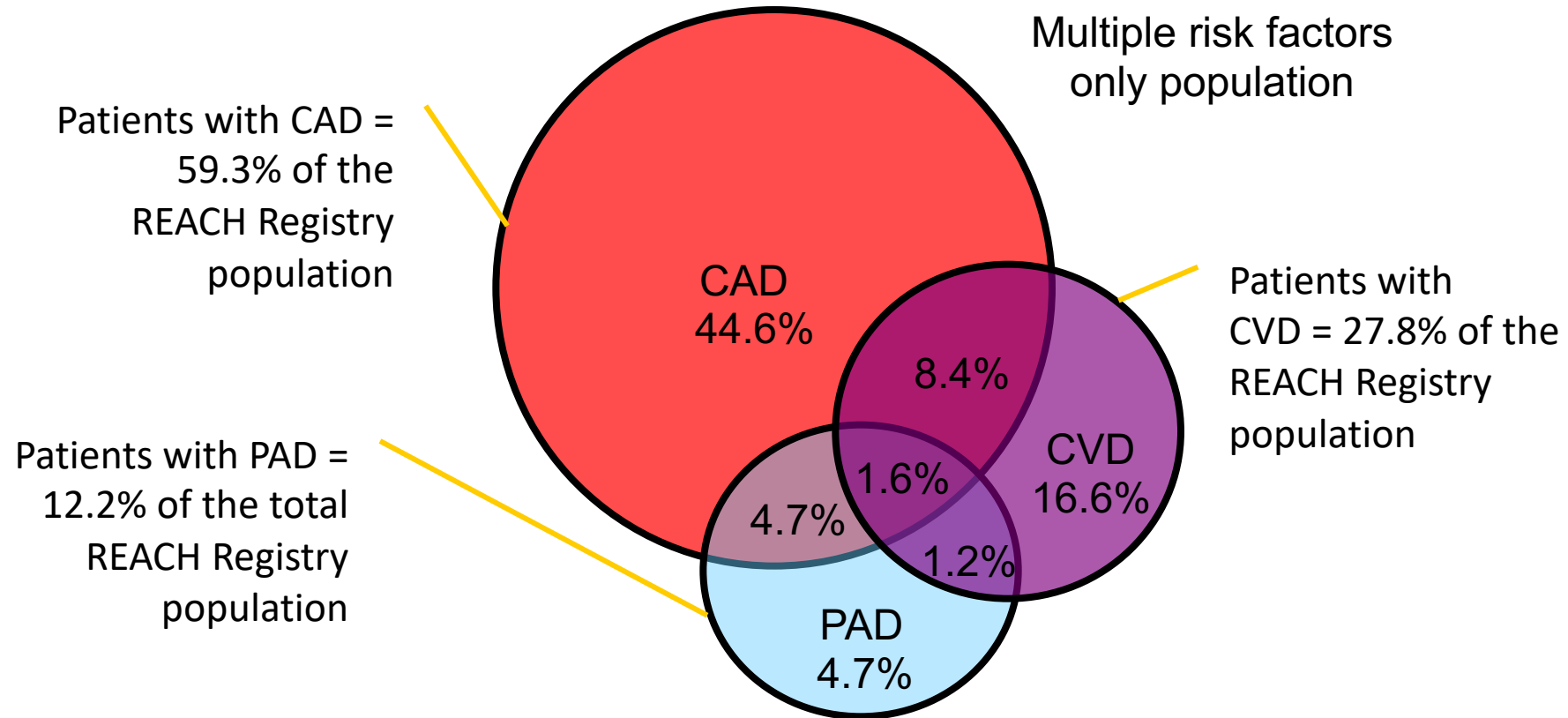
Bonaca, MP. JACC 2016; 67(23):2719-2728

Polyvascular Disease increases MACE risk in PAD

- **Polyvascular is symptomatic atherosclerotic disease in more than one vascular bed**
- **Coronary**
- **Peripheral**
- **Cerebral**

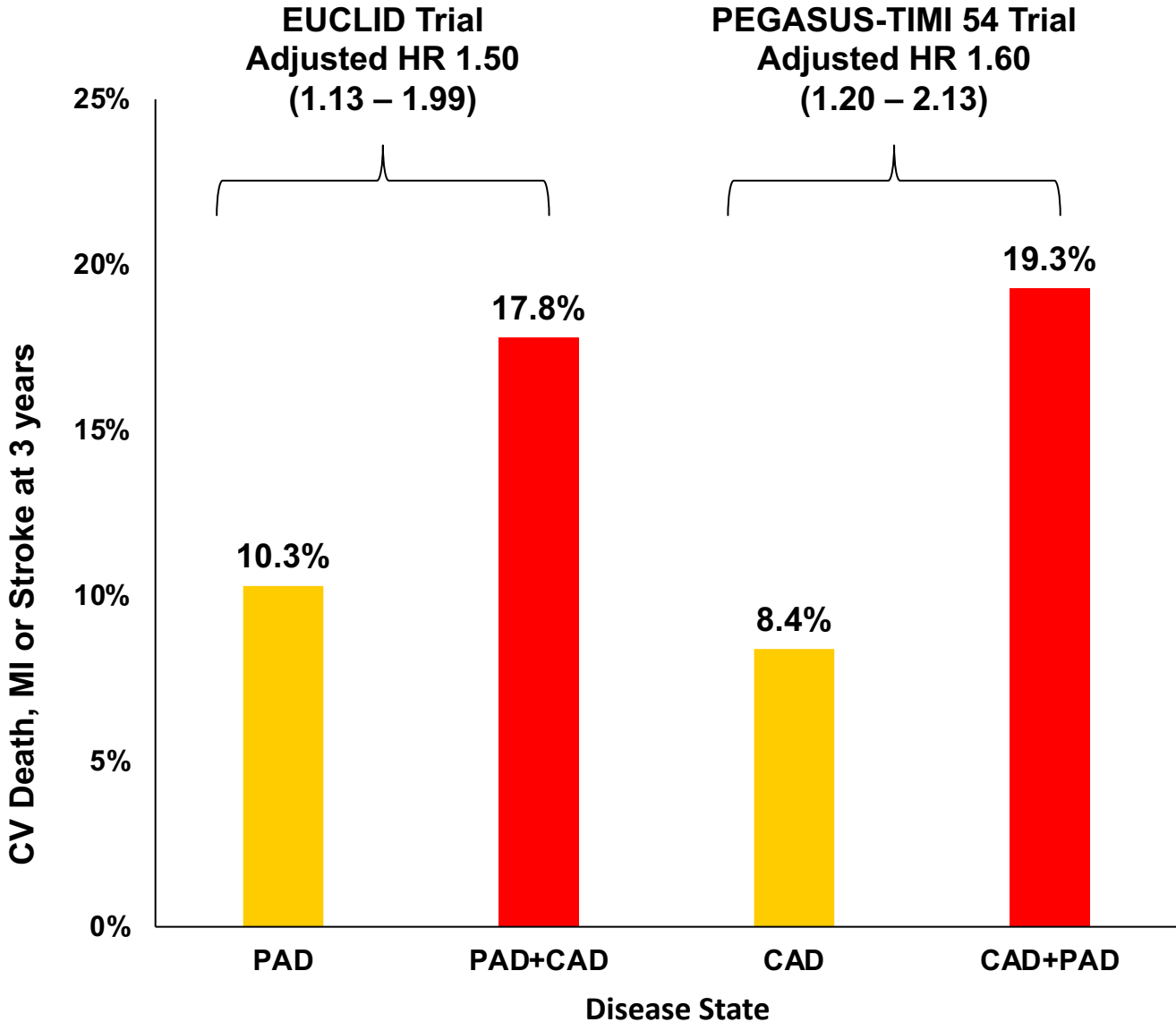
A large proportion of atherothrombosis patients have polyvascular disease in REACH registry

Approximately 1 / 6 of the 55,499 patients with symptomatic atherothrombosis suffered the disease in multiple arterial territories



CAD, coronary artery disease; CVD, cerebrovascular disease; PAD, peripheral artery disease.
Bhatt DL et al, on behalf of the REACH Registry Investigators. JAMA 2006;295:180-189.

Polyvascular Disease in PAD is Associated with Increased MACE Risk



Bonaca MP Vasc Med 2018;23:531-33.

Outcomes in PAD Summary

- **Increased Mortality**
- **Increased events**
- **MALE greater than MACE in overall PAD populations**
- **MALE further enhanced by**
 - **Lower ABI**
 - **Prior Revascularization**
- **MACE further enhanced by**
 - **Prior MACE**
 - **Polyvascular disease**