

# **PERIPHERAL ARTERIAL DISEASE**

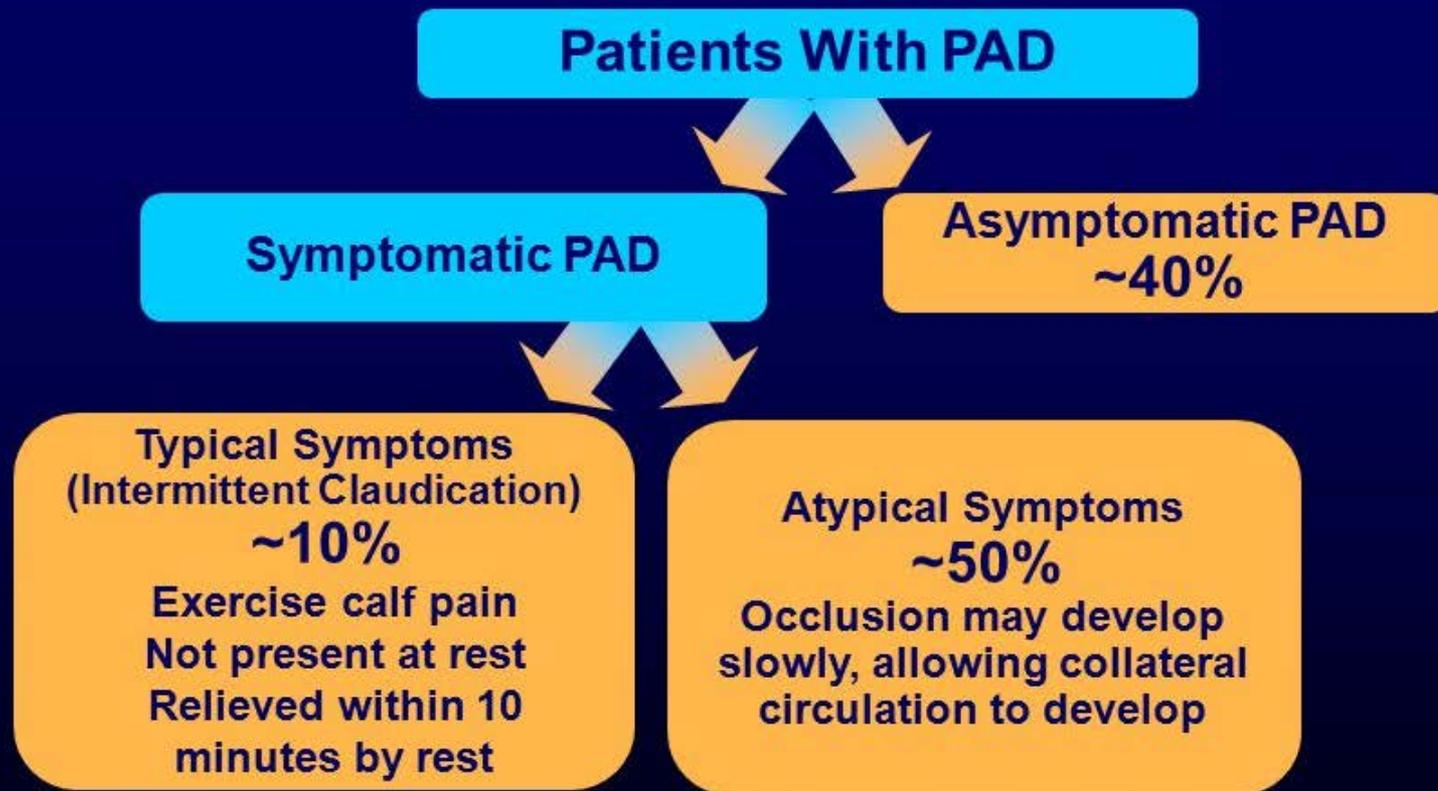
**ASIF MAHMOOD MD FRCS**

**CONSULTANT VASCULAR SURGEON**

# OBJECTIVES

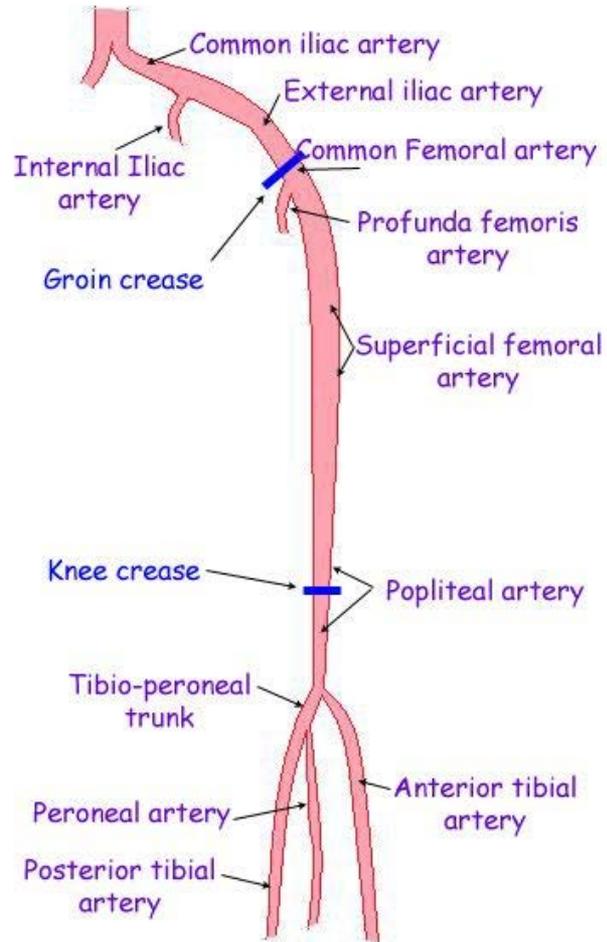
- **RECOGNISING PAD**
- **IMPORTANCE OF PAD**
- **NICE GUIDANCE AND MEDICAL MANAGEMENT**
- **REVASCULARISATION**
- **WOUNDS**
- **CASES**

# PAD: Symptoms



American Heart Association. *Heart Disease and Stroke Statistics—2005 Update*. 2005; Criqui MH et al. *Vasc Med*. 1996;1:65-71.

# LEVELS OF DISEASE



# DIFFERENTIAL DIAGNOSIS

## CLAUDICATION

- Neurogenic/ Spinal
- Deep venous claudication
- Chronic compartment syndrome
- Musculo-skeletal

## CRITICAL ISCHAEMIA

- Small vessel disease
  - Vasospastic
  - Vasculitis
  - Micro-embolism
  - Musculo-skeletal



# ISCHAEMIC ULCER





# Mixed Ulcers

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**Sepsis**



**Neuropathy**



**Venous Disease**

# HAND-HELD DOPPLER



**Table 1 – Interpretation of ABI ratios**

<b>ABI</b>	<b>Severity</b>	<b>Claudication</b>
>1.30	Noncompressible vessel	Present
1.00-1.29	Normal	None
0.91-0.99	Borderline (equivocal)	None
0.41-0.90	Mild to moderate PAD	Present late, limiting
0.00-0.40	Severe PAD	Early, limiting

ABI, ankle-brachial index; PAD, peripheral arterial disease.

# Evaluating the evidence for management of CLI: Limitations of ankle pressures

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- **30-40% in most clinical series**
- **Diabetics**
  - >80 yrs old**
  - Renal failure**
  - Severe induration**
- **Pole test**
  - Toe pressure**



# TASC

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## *Recommendation 74*

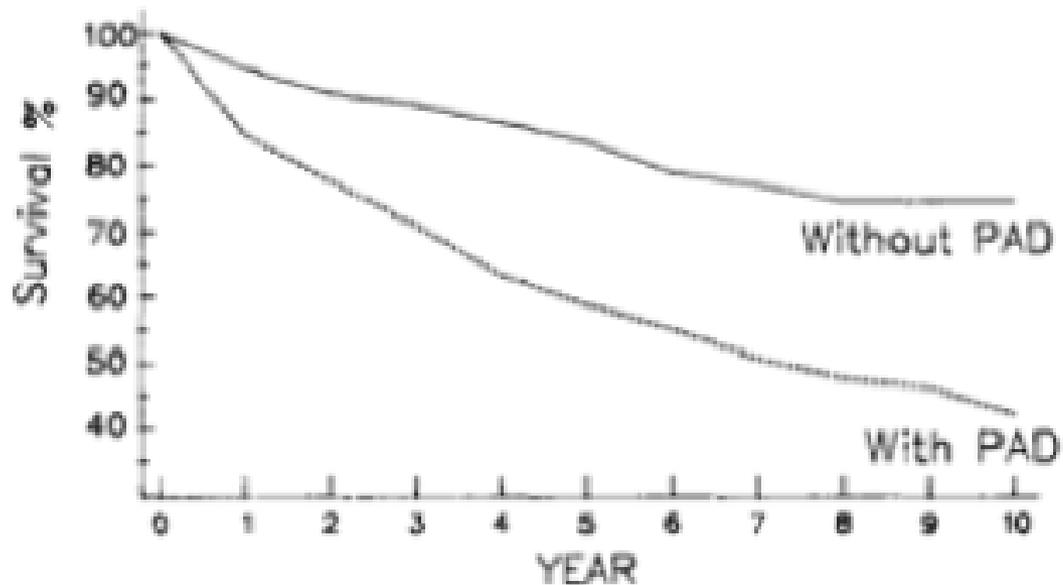
- **Rest pain / tissue loss with:**

  - AP < 50-70 mm Hg**

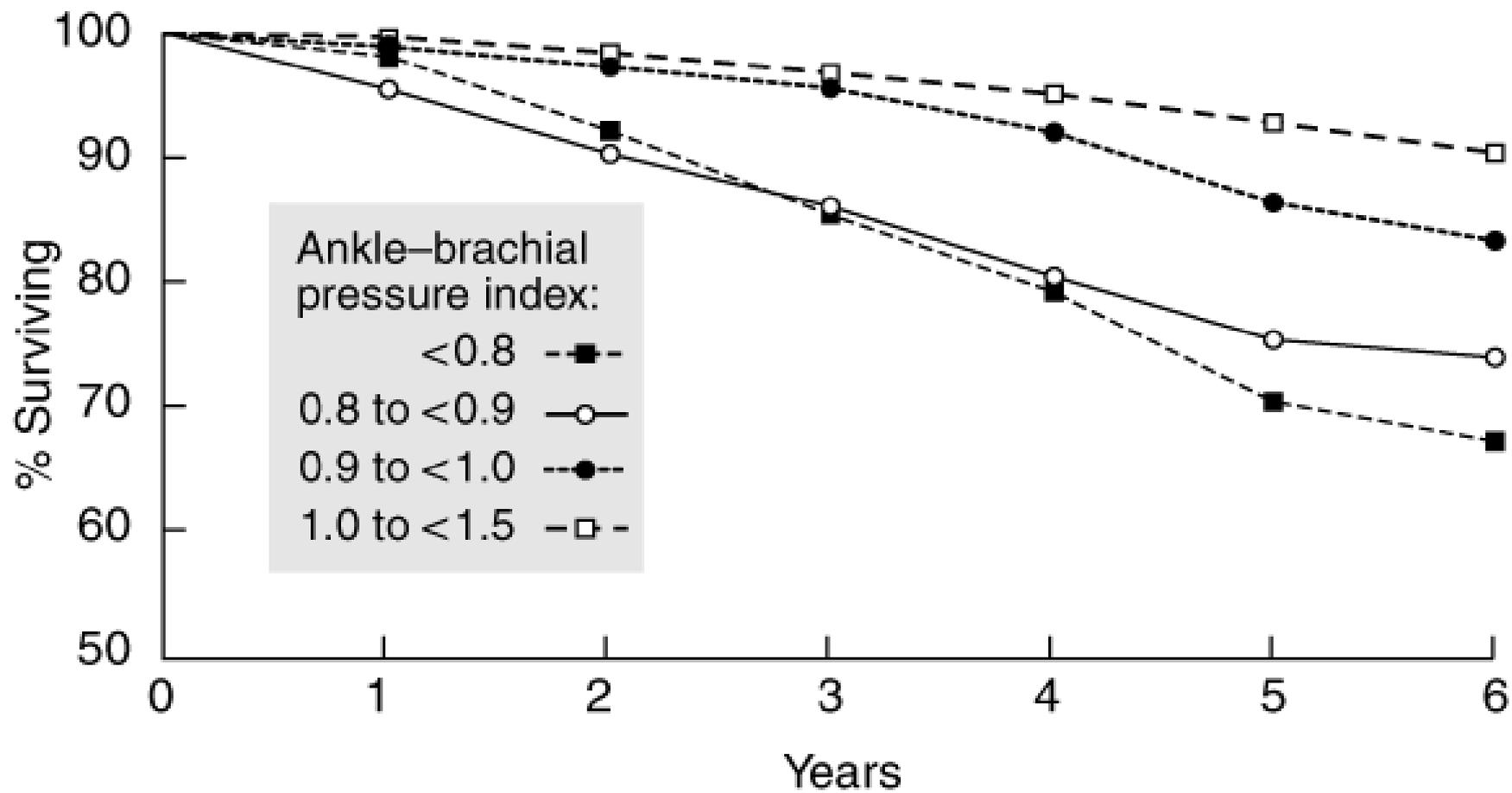
  - TP < 30-50 mm Hg**

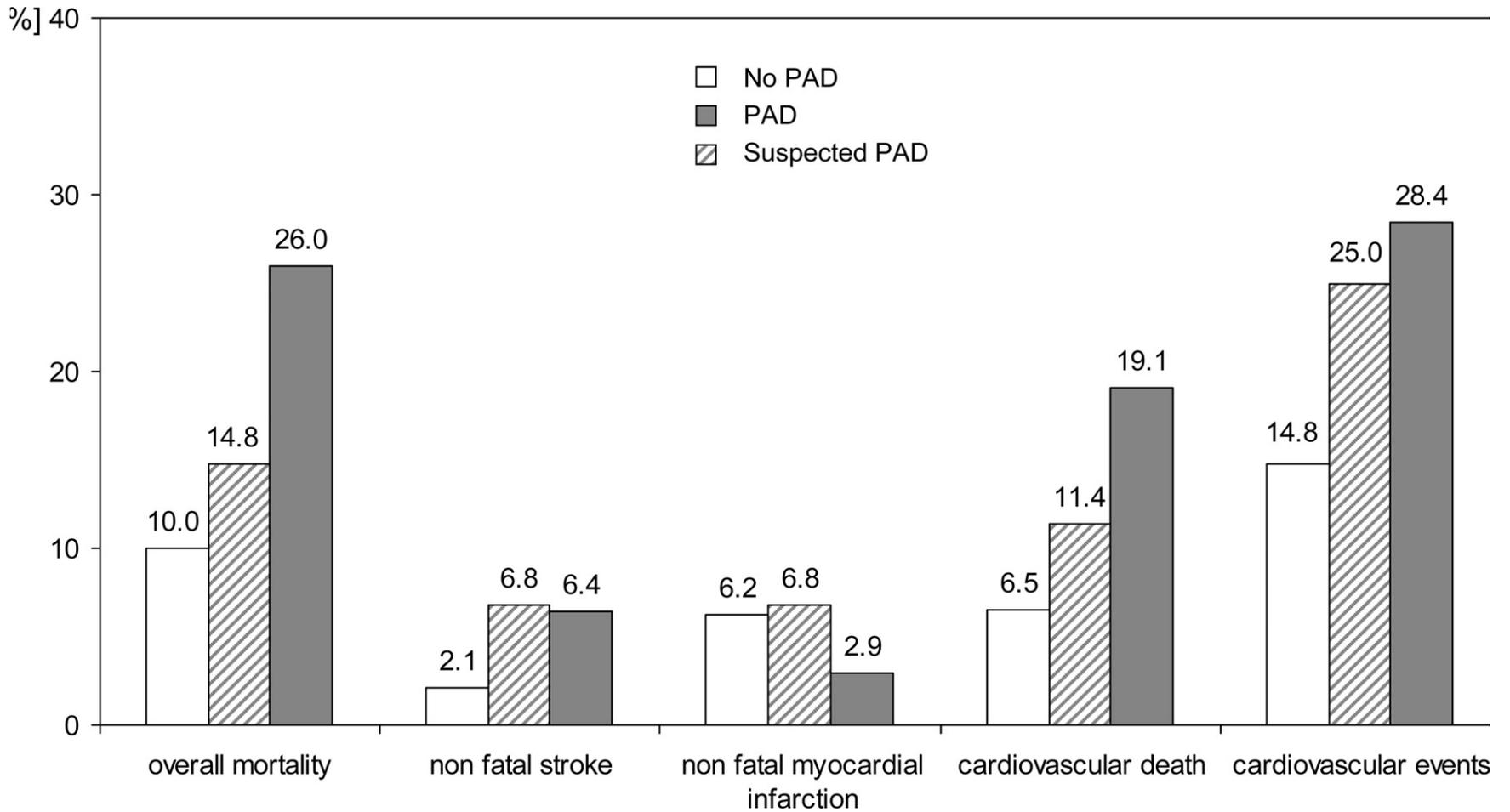
  - TcPO<sub>2</sub> < 30-50 mm Hg**

- **“Major amputation required within next 6-12 months in absence of significant haemodynamic improvement..”**



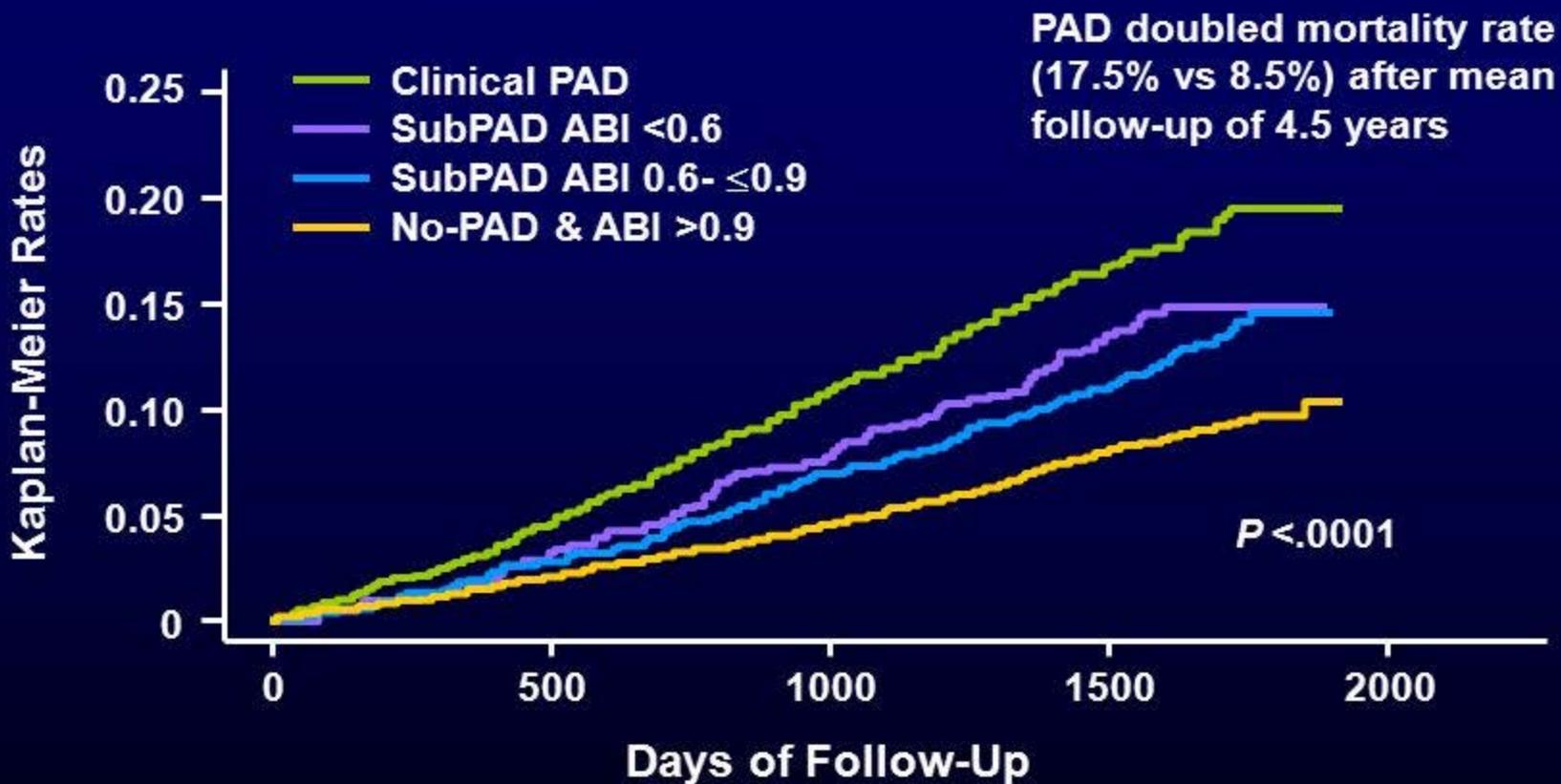
**Figure 1.** Patients with peripheral artery disease have lower survival rates than patients without peripheral artery disease. Reprinted with permission from *Atherosclerosis*.<sup>4</sup> Copyright 1991, Elsevier.





# HOPE

## PAD: Increased Risk of Mortality



HOPE = Heart Outcomes Prevention Evaluation.  
Ostergren J et al. *Eur Heart J*. 2004;25:17-24.

# CRITICAL ISCHAEMIA

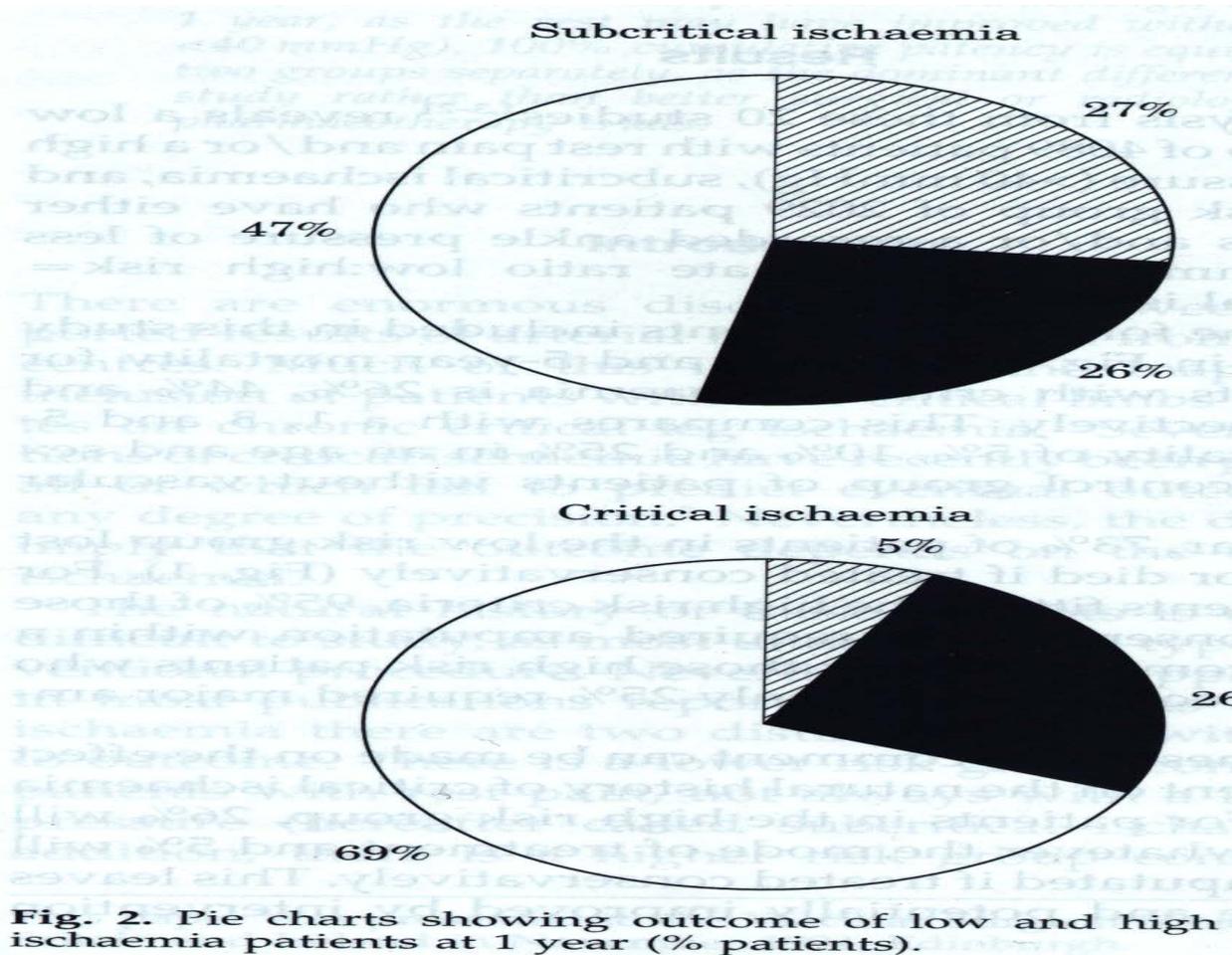
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- **Incidence: European Working Group: 500-1000/ million per year**
- **Annual Prevalence: VSSGBI: 1 in 2500 of which 30% were diabetic**
- **50,000 admissions in England and Wales per year of which 15,000 have major surgery including amputation**
- **50% die within 5 years of presentation**

# Critical and Subcritical Ischaemia

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**Fig. 2.** Pie charts showing outcome of low and high ischaemia patients at 1 year (% patients).

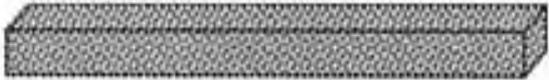
# Is revascularisation worth it?

*Wheelchair or bed bound*

*Amputees*  *38%*

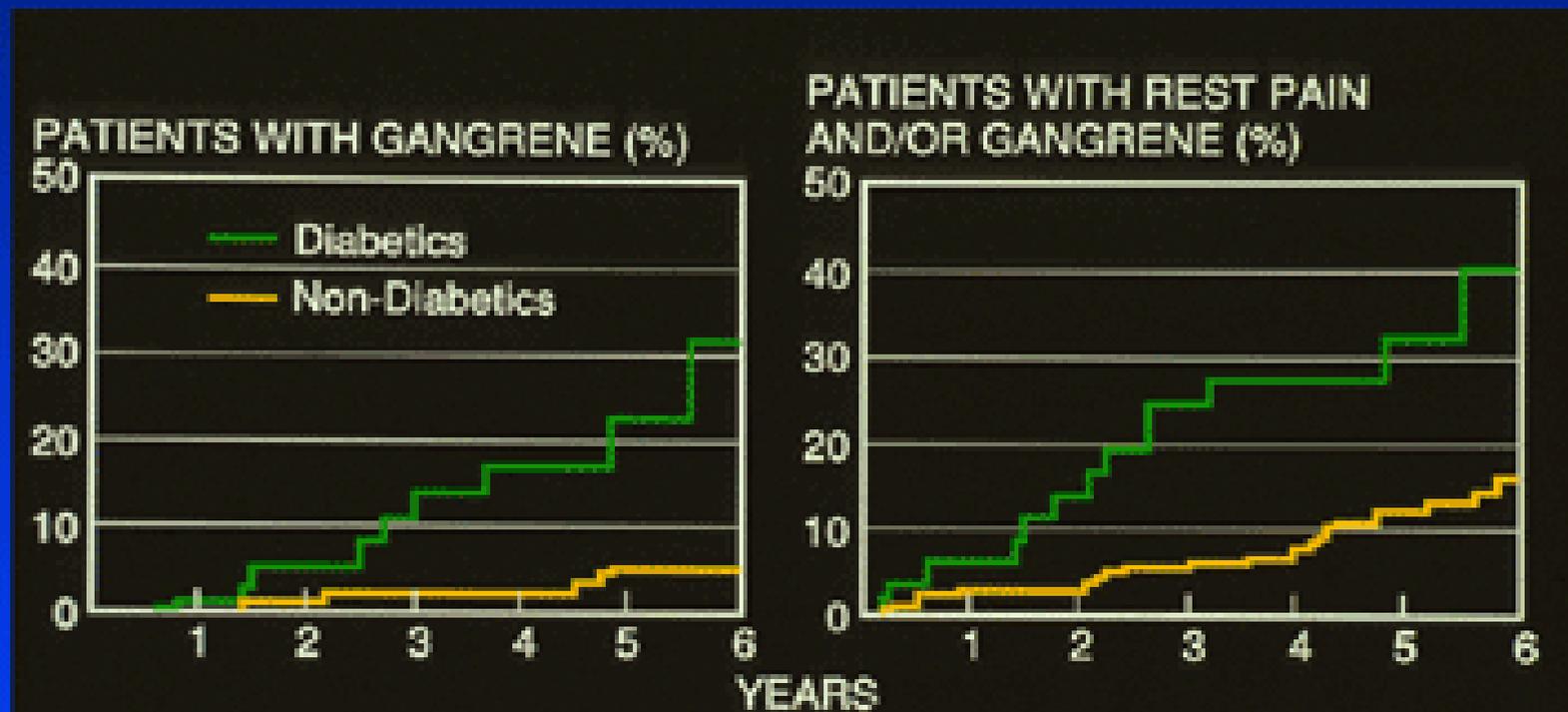
*Reconstructions*  *13%*

*Mobile outside the home*

*Amputees*  *31%*

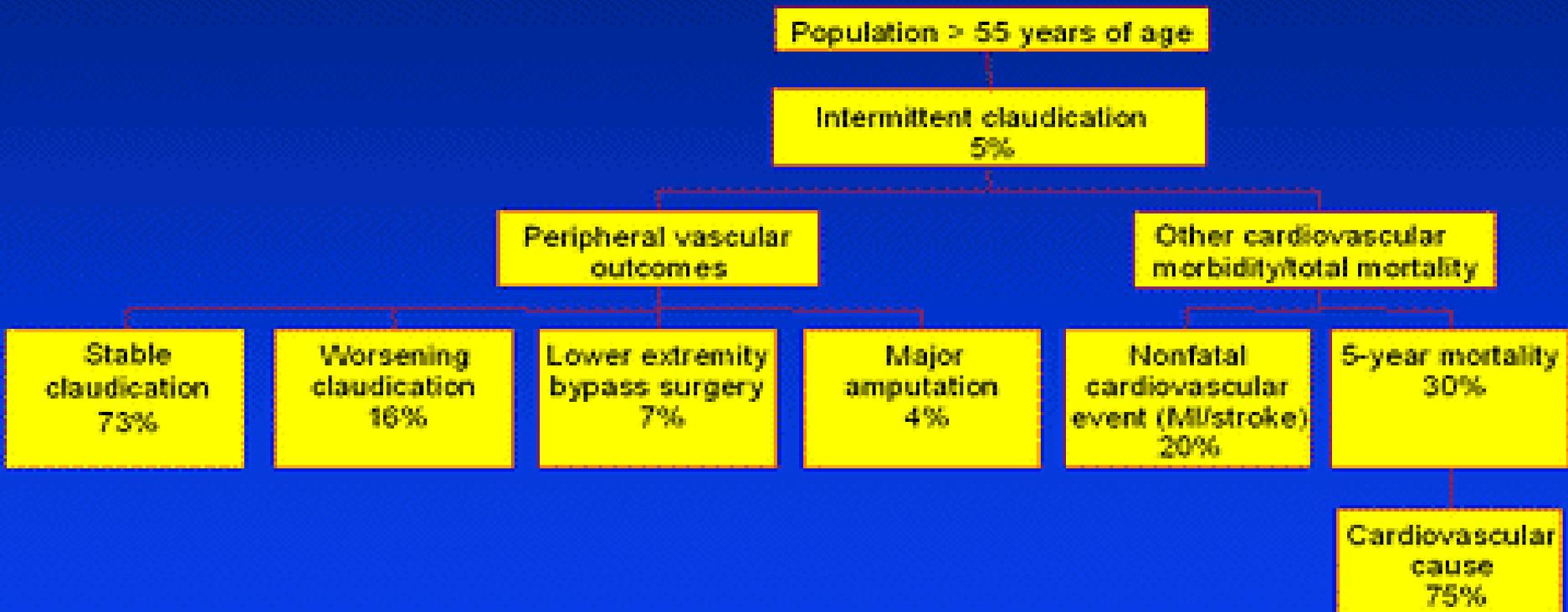
*Reconstructions*  *52%*

# Fate of the Limb in Peripheral Arterial Disease



Reprinted with permission from Jonason T et al. *Acta Med Scand.* 1985;218:217

# Natural History of Intermittent Claudication



Adapted with permission from Weitz JI et al. *Circulation*. 1996;94:3026

# NICE GUIDANCE

# NICE quality standard calls for early identification of PAD

- 22 January 2014
- NICE is calling for early identification of asymptomatic and symptomatic peripheral arterial disease to help improve the care of patients with the condition.
- Peripheral arterial disease (PAD) is a common condition affecting around a fifth of people over the age of 60. People with PAD are approximately 3-4 times more likely to have a cardiovascular morbidity and mortality than those without the condition, even if the disease is asymptomatic.
- **Primary care professionals should ensure that any comprehensive assessment includes both a clinical assessment with structured history taking, and ABPI measurement with a hand-held doppler ultrasound scan to ensure an accurate diagnosis and quantification of disease severity.**

# NICE quality standard [QS52]

Published date: January 2014

- **Statement 1. People who have symptoms of, or who are at risk of developing, peripheral arterial disease (PAD) are offered a clinical assessment and ankle brachial pressure index (ABPI) measurement.**
- **Statement 2. People with PAD are offered an assessment for cardiovascular comorbidities and modifiable risk factors.**
- **Statement 3. People with intermittent claudication are offered a supervised exercise programme.**
- Statement 4. People with PAD being considered for revascularisation who need further imaging after a duplex ultrasound are offered magnetic resonance angiography (MRA).
- Statement 5. People with intermittent claudication are offered angioplasty only when imaging has confirmed it is appropriate, after advice on the benefits of modifying risk factors has been given and after a supervised exercise programme has not improved symptoms.

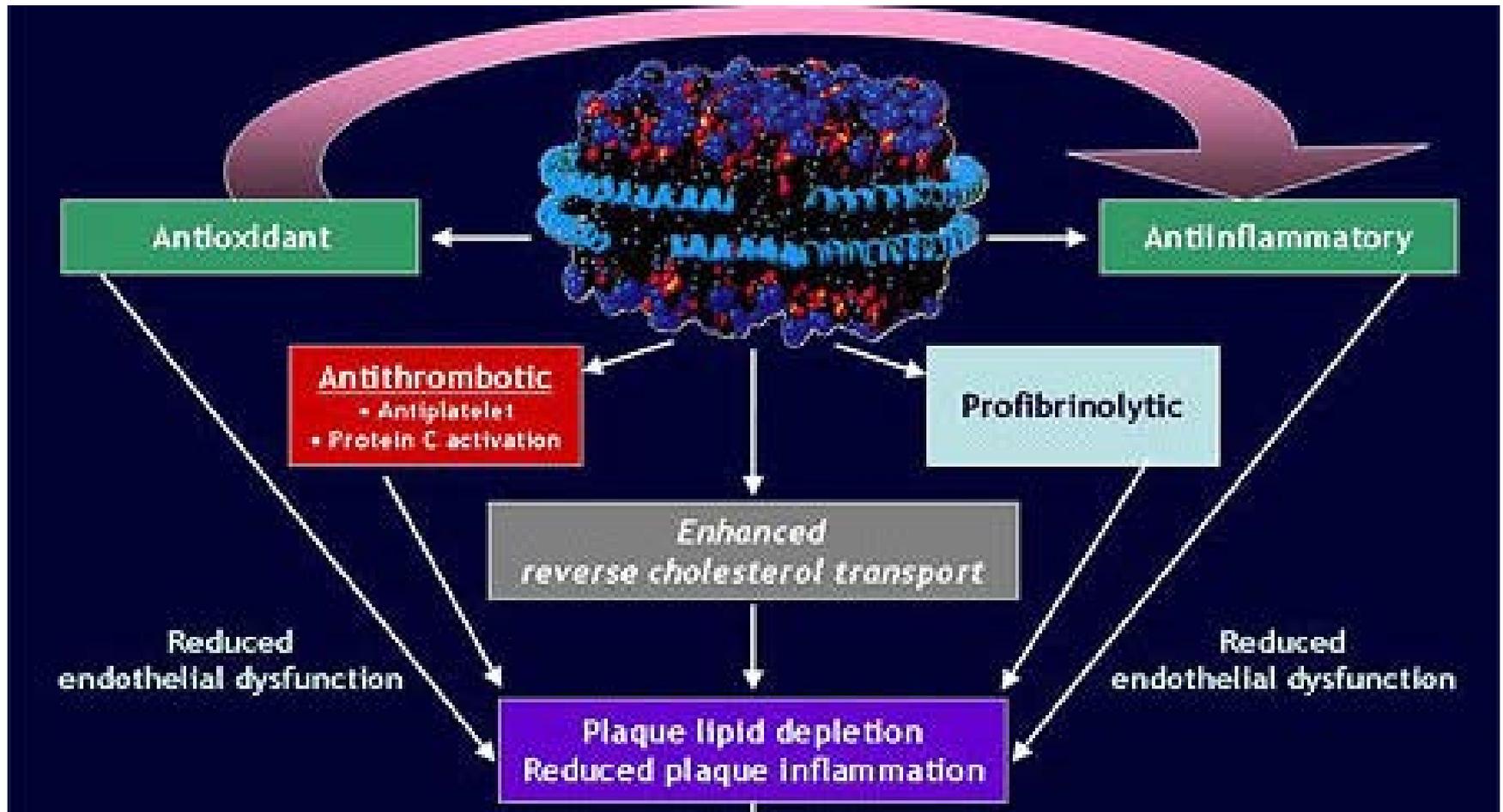
# EARLY DETECTION OF PAD

- Assess people for the presence of peripheral arterial disease if they:
  - have symptoms suggestive of peripheral arterial disease or
  - have diabetes, non-healing wounds on the legs or feet or unexplained leg pain or
  - are being considered for interventions to the leg or foot or
  - need to use compression hosiery.

# CVS MANAGEMENT

- **The assessment of cardiovascular comorbidities and modifiable risk factors should include a review of**
- **smoking status**
- **diet**
- **weight**
- **cholesterol levels**
- **presence of diabetes**
- **presence of hypertension**
- **current antiplatelet therapy**
- [Adapted from NICE clinical guideline 147, recommendation 1.2.1]

# PLEIOTROPIC EFFECTS OF STATINS



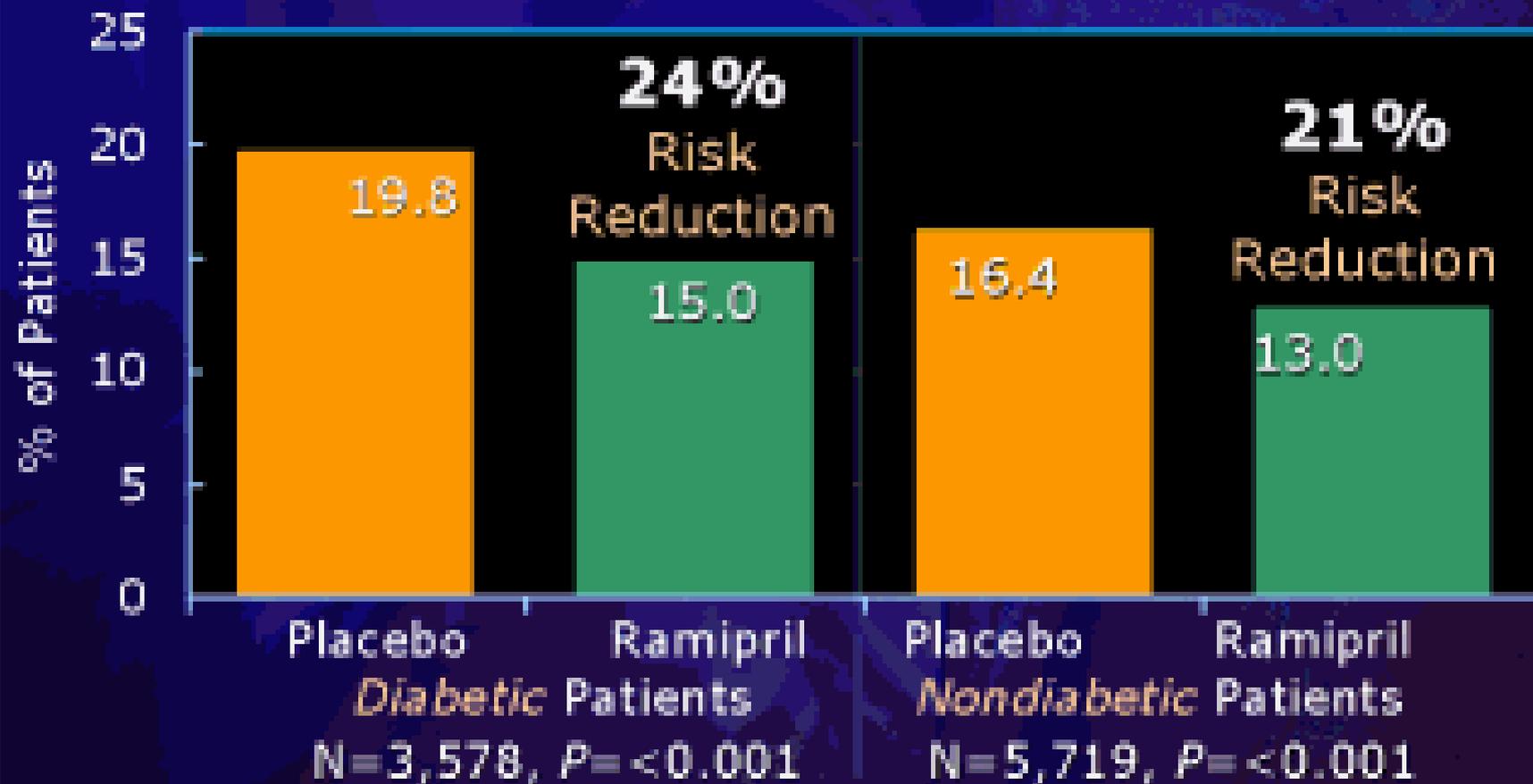
# Which anti-platelet

- Clopidogrel 75 mg daily is the preferred antiplatelet.
- If clopidogrel is contraindicated or not tolerated, give low dose aspirin alone.
- If both clopidogrel and aspirin are contraindicated or not tolerated, give modified-release dipyridamole alone.

# ACE-I & ARB's are beneficial in normotensive atherosclerotic patients

- 13 trials of 80,594 patients; outcomes included 5674 CV deaths, 3106 MIs, and 4452 strokes.
- ACE-I or ARB reduced these by 11% (95% CI 7–15%), with no variation in efficacy across baseline BP strata.
- In patients with baseline SBP <130 mmHg, ACE-I or ARB reduced the composite primary outcome by 16% (10–23%)

# Heart Outcomes Prevention Evaluation (HOPE) Study Effect of Ramipril on Cardiovascular Events (Myocardial Infarction, Stroke, or CVD Death) ~ 4.5 Yrs



# TREATING SYMPTOMS OF CLAUDICATION

## Exercise

- If available, offer a supervised exercise programme to all people with two hours of supervised exercise a week for a 3-month period.
  - Encouraging people to exercise to the point of maximal pain.
- If supervised exercise is not available, consider suggesting unsupervised exercise (using clinical judgement and taking into account the person's motivation and comorbidities).
  - This involves advice to exercise for approximately 30 minutes three to five times per week, walking until the onset of symptoms, then resting to recover.

## Refer for consideration of angioplasty or bypass surgery when:

- Advice on the benefits of modifying risk factors has been reinforced, *and*
- A supervised exercise programme has not led to a satisfactory improvement in symptoms.

## Consider prescribing naftidrofuryl oxalate if:

- Supervised exercise has not led to a satisfactory improvement, *and*
- The person prefers not to be referred for consideration of angioplasty or bypass surgery.
- Review progress after 3–6 months and discontinue naftidrofuryl oxalate if there has been no symptomatic benefit.

## Offer advice on driving:

- If the person holds a bus, coach, or lorry licence, advise them that they should inform the Driver and Vehicle Licensing Agency (DVLA) about their peripheral arterial disease. Relicensing may be permitted if there is no symptomatic myocardial ischaemia and exercise and functional requirements can be met.
- Drivers with a car or motorcycle licence do not need to tell the DVLA. However, taxi drivers should inform their local authority who have responsibility for determining standards (including medical requirements) over and above the driver licensing requirements.

# STATINS IMPROVE PAD

## AIMS:

Due to a high burden of systemic cardiovascular events, current guidelines recommend the use of statins in all patients with peripheral artery disease (PAD). We sought to study the impact of statin use on limb prognosis in patients with symptomatic PAD enrolled in the international REACH registry.

## METHODS:

Statin use was assessed at study enrolment, as well as a time-varying covariate. Rates of the primary adverse limb outcome (worsening claudication/new episode of critical limb ischaemia, new percutaneous/surgical revascularization, or amputation) at 4 years and the composite of cardiovascular death/myocardial infarction/stroke were compared among statin users vs. non-users.

## RESULTS:

**A total of 5861 patients with symptomatic PAD were included.** Statin use at baseline was 62.2%. Patients who were on statins had a significantly lower risk of the primary adverse limb outcome at 4 years when compared with those who were not taking statins [22.0 vs. 26.2%; hazard ratio (HR), 0.82; 95% confidence interval (CI), 0.72-0.92; P = 0.0013]. Results were similar when statin use was considered as a time-dependent variable (P = 0.018) and on propensity analysis (P < 0.0001). The composite of cardiovascular death/myocardial infarction/stroke was similarly reduced (HR, 0.83; 95% CI, 0.73-0.96; P = 0.01).

## CONCLUSION:

**Among patients with PAD in the REACH registry, statin use was associated with an ~18% lower rate of adverse limb outcomes, including worsening symptoms, peripheral revascularization, and ischaemic amputations.**

These findings suggest that statin therapy not only reduces the risk of adverse cardiovascular events, but also favourably affects limb prognosis in patients with PAD.

Eur Heart J. 2014 Nov 1;35(41):2864-72. doi: 10.1093/eurheartj/ehu080. Epub 2014 Feb 28.

- **Statin therapy and long-term adverse limb outcomes in patients with peripheral artery disease: insights from the REACH registry.**
- [Kumbhani DJ1, Steg PG2, Cannon CP3, Eagle KA4, Smith SC Jr5, Goto S6, Ohman EM7, Elbez Y8, Sritara P9, Baumgartner I10, Banerjee S11, Creager MA12, Bhatt DL13; REACH Registry Investigators.](#)

# PHARMACOLOGICAL TREATMENT

- **Naftidrofuryl oxalate**
- This recommendation is based on the consensus of the NICE GDG who considered evidence from 5 RCTs included in a NICE technology appraisal [NICE, 2011], and a **Cochrane systematic review of 7 RCTs** [de Backer et al, 2012].
- The conclusions were that naftidrofuryl oxalate improves maximal and pain-free walking distance when compared with placebo, cilostazol, and pentoxifylline. However, the NICE GDG noted that these distances were shorter than the distance they considered minimally important for their guideline.
- Evidence from a Cochrane systematic review [de Backer et al, 2012] enabled the calculation of a number needed to treat of 4.5 for naftidrofuryl oxalate. This means that for every 4.5 people treated, one will experience benefit.

# ACE INHIBITORS IMPROVE WALKING DISTANCE

## OBJECTIVE:

To determine the efficacy of ramipril for improving walking ability, patient-perceived walking performance, and quality of life in patients with claudication.

## DESIGN, SETTING, AND PATIENTS:

**Randomized, double-blind, placebo-controlled trial conducted among 212 patients with peripheral artery disease** (mean age, 65.5 [SD, 6.2] years), initiated in May 2008 and completed in August 2011 and conducted at 3 hospitals in Australia.

## INTERVENTION:

Patients were randomized to receive 10 mg/d of ramipril (n = 106) or matching placebo (n = 106) for 24 weeks.

## MAIN OUTCOME MEASURES:

Maximum and pain-free walking times were recorded during a standard treadmill test. The Walking Impairment Questionnaire (WIQ) and Short-Form 36 Health Survey (SF-36) were used to assess walking ability and quality of life, respectively.

## RESULTS:

At 6 months, relative to placebo, ramipril was associated with a 75-second (95% CI, 60-89 seconds) increase in mean pain-free walking time (P < .001) and a 255-second (95% CI, 215-295 seconds) increase in maximum walking time (P < .001). Relative to placebo, ramipril improved the WIQ median distance score by 13.8 (Hodges-Lehmann 95% CI, 12.2-15.5), speed score by 13.3 (95% CI, 11.9-15.2), and stair climbing score by 25.2 (95% CI, 25.1-29.4) (P < .001 for all). The overall SF-36 median Physical Component Summary score improved by 8.2 (Hodges-Lehmann 95% CI, 3.6-11.4; P = .02) in the ramipril group relative to placebo. Ramipril did not affect the overall SF-36 median Mental Component Summary score.

## CONCLUSIONS AND RELEVANCE:

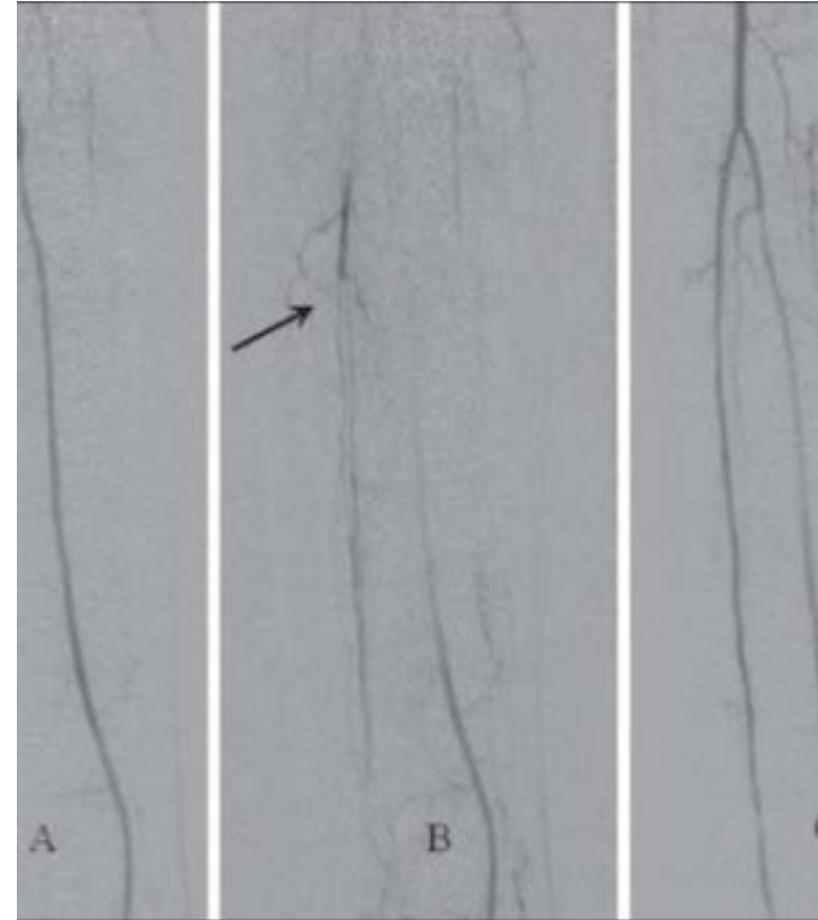
**Among patients with intermittent claudication, 24-week treatment with ramipril resulted in significant increases in pain-free and maximum treadmill walking times compared with placebo.** This was associated with a significant increase in the physical functioning component of the SF-36 score.

JAMA. 2013 Feb 6;309(5):453-60. doi: 10.1001/jama.2012.216237.

**Effect of ramipril on walking times and quality of life among patients with peripheral artery disease and intermittent claudication: a randomized controlled trial.**

[Ahimastos AA1, Walker PJ, Askew C, Leicht A, Pappas E, Blombery P, Reid CM, Golledge J, Kingwell BA.](#)

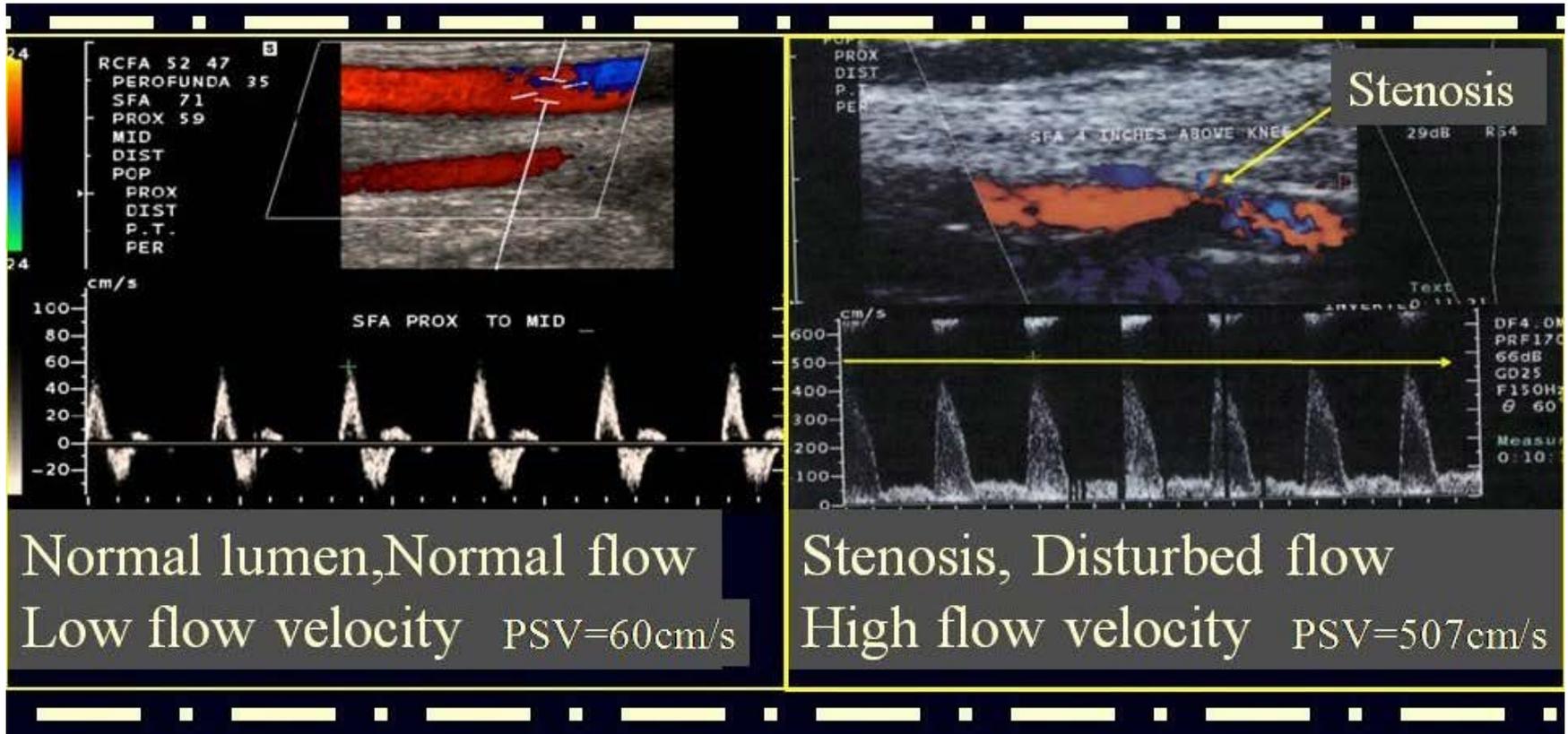
# REVASCULARISATION



# Revascularization Strategies in CLI: Key Factors in Decision-Making

- General health of the patient
  - Age, comorbidities, ambulatory status
- Foot: likelihood of functional salvage
- Severity of limb ischemia
- Anatomic distribution of disease
- Prior vascular interventions
- Availability of autogenous vein for LEB
  - Ipsilateral GSV > contralateral GSV > alternative veins
  - Prosthetics and other non-autogenous conduits inferior

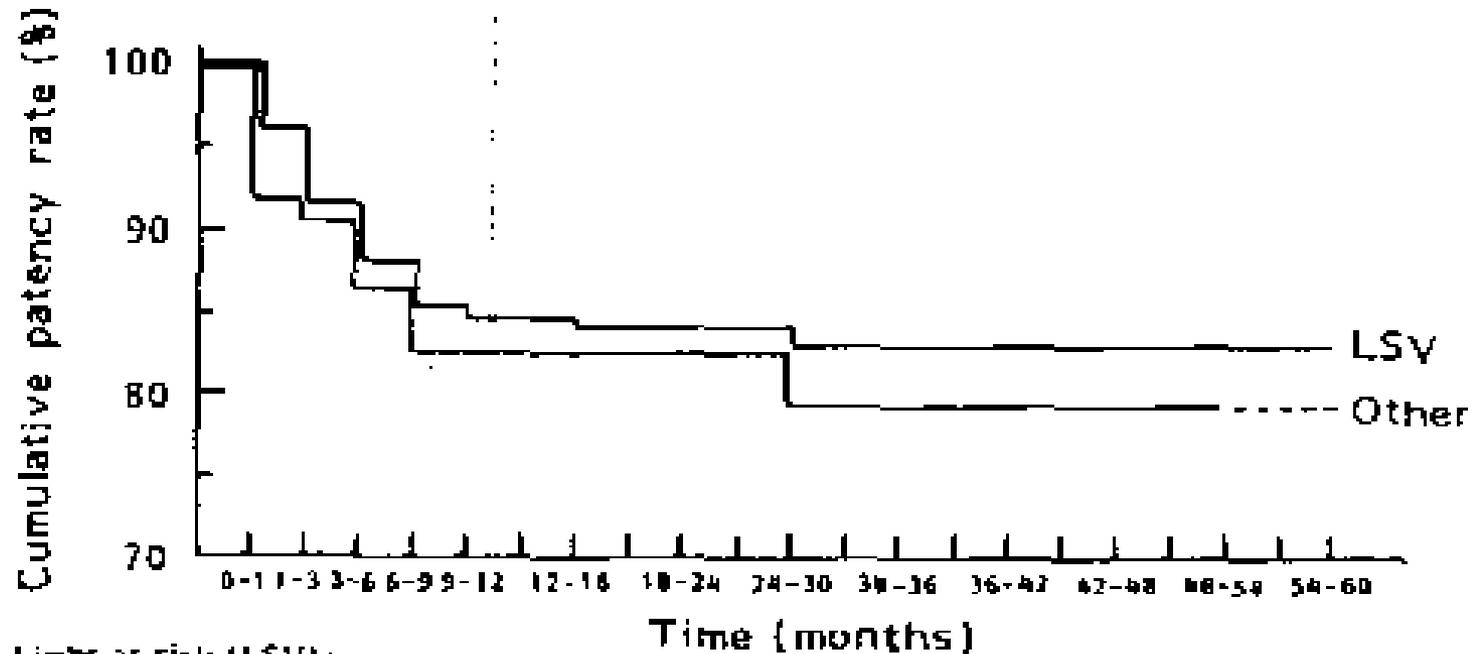
# DUPLEX ULTRASOUND



# Aggressive arterial reconstruction for critical lower limb ischaemia

Hickey NC, Thomson IA, Shearman CP, Simms MH.

Br J Surg. 1991 Dec;78(12):1476-8.



Limbs at risk (LSV):

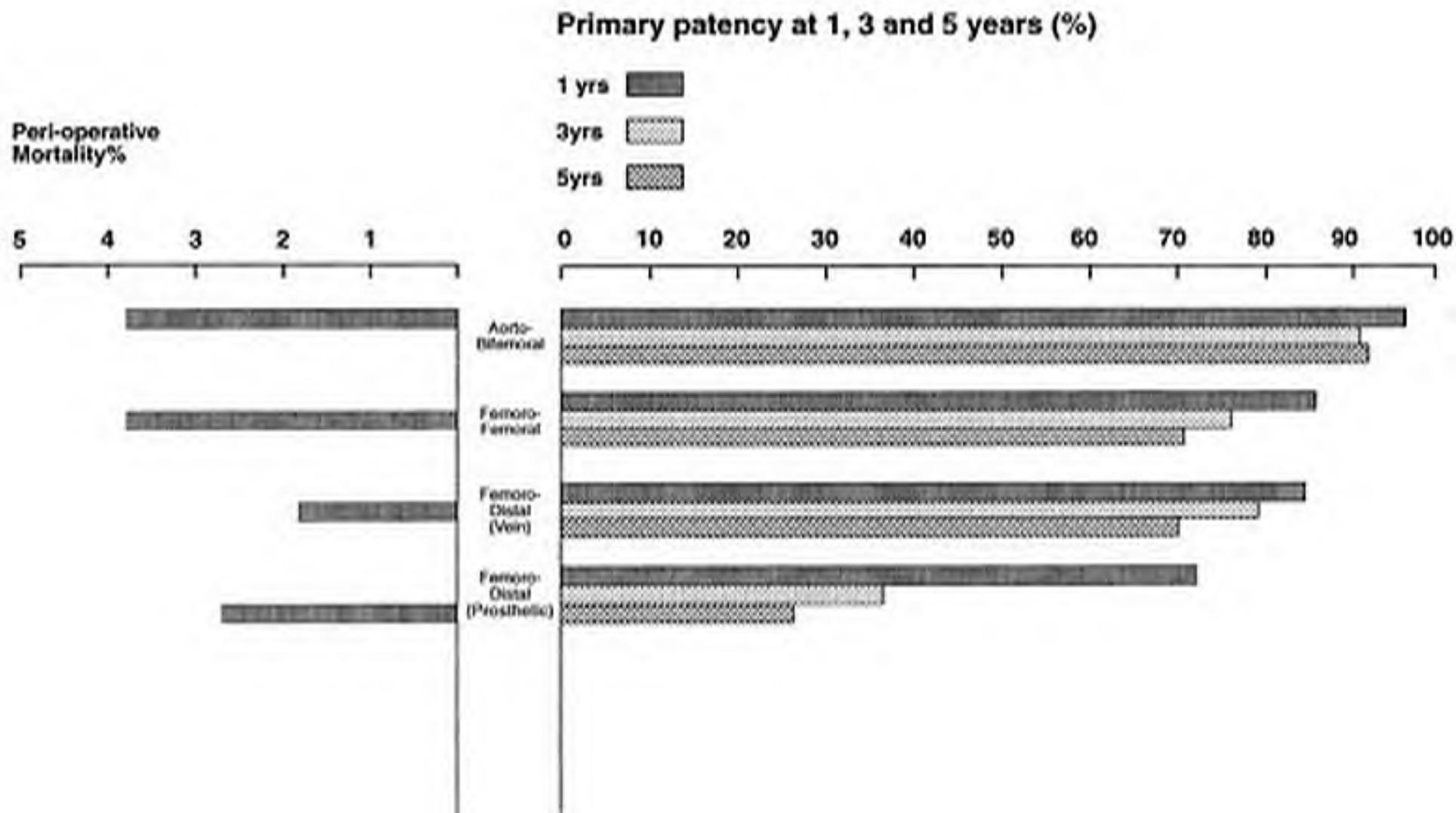
179 158 143 136 124 115 94 79 61 52 34 28 22

Limbs at risk (Other):

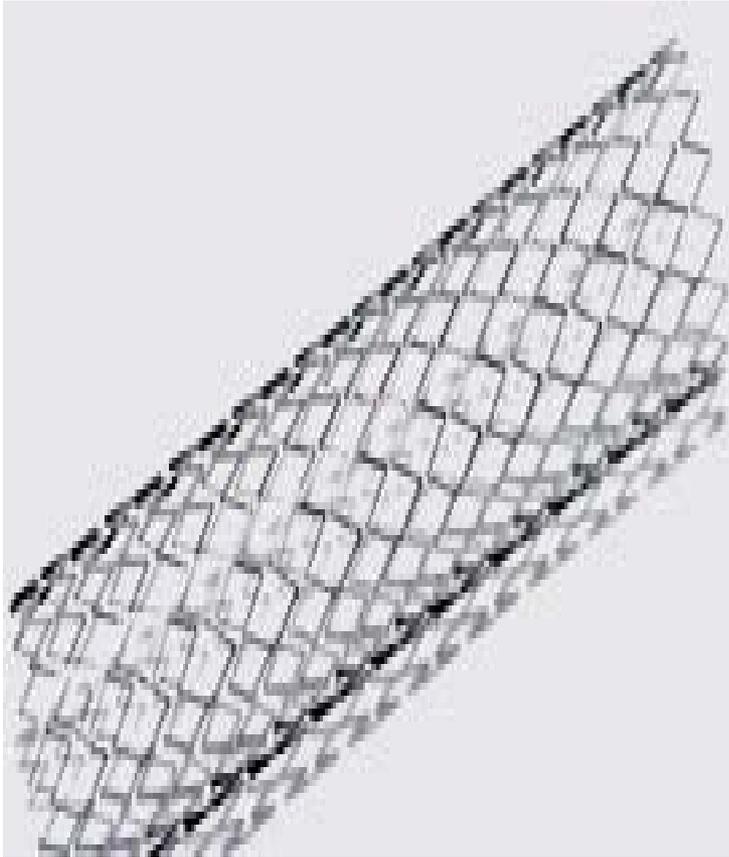
60 53 48 45 42 40 34 24 25 20 16 11 6

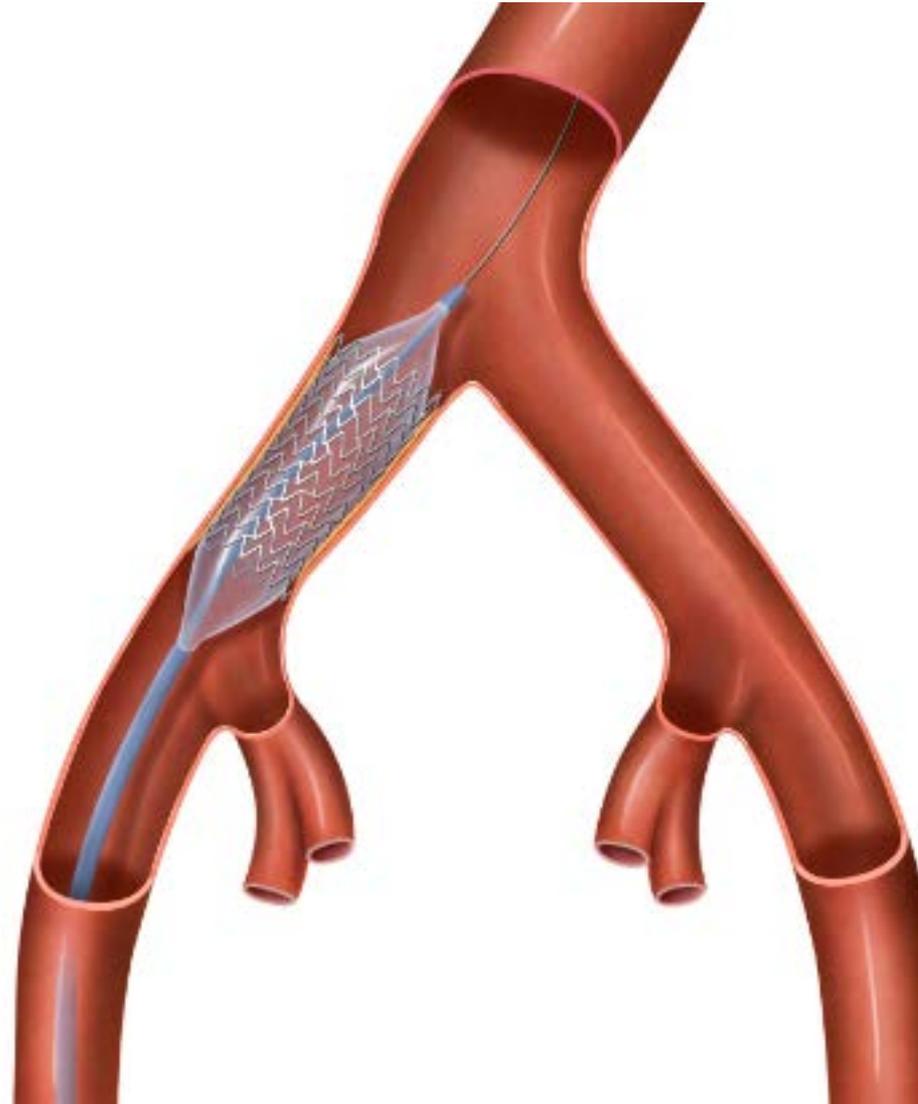
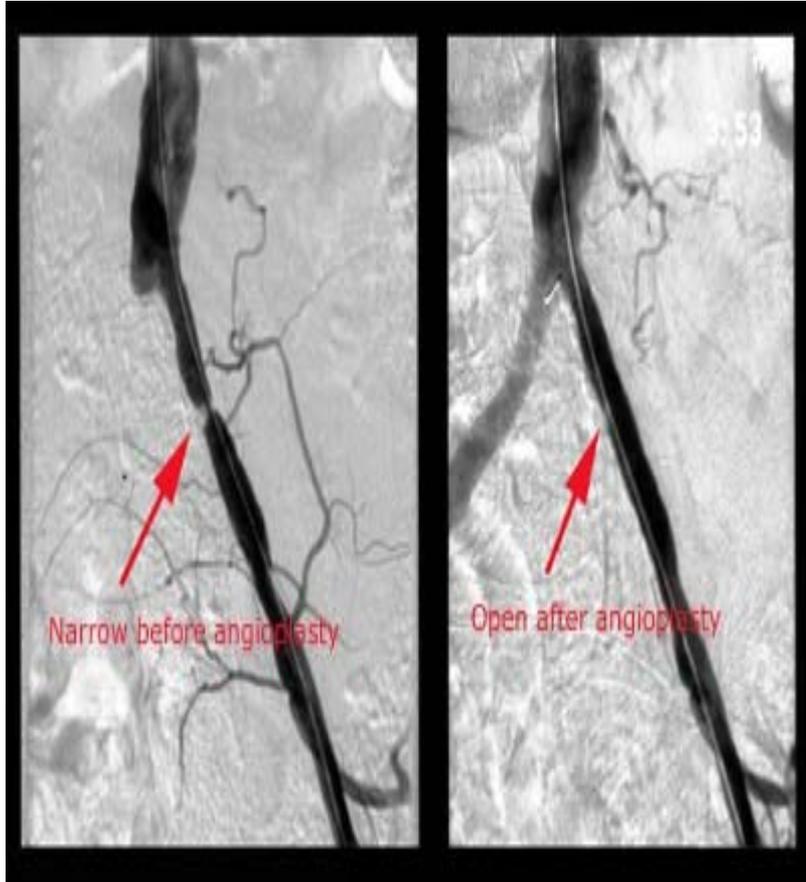
# Average results for surgical treatment

- Pooled weighted data from tables 41, 43, 44, and 45
- Only studies with over 50% CLI patients included

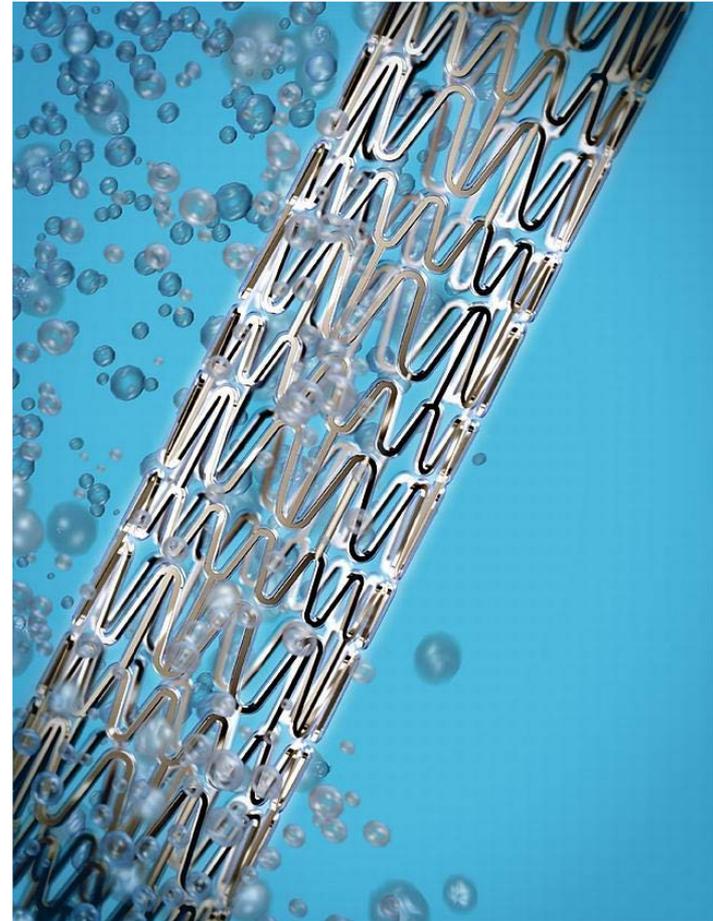
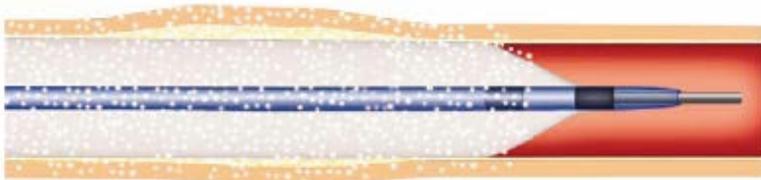


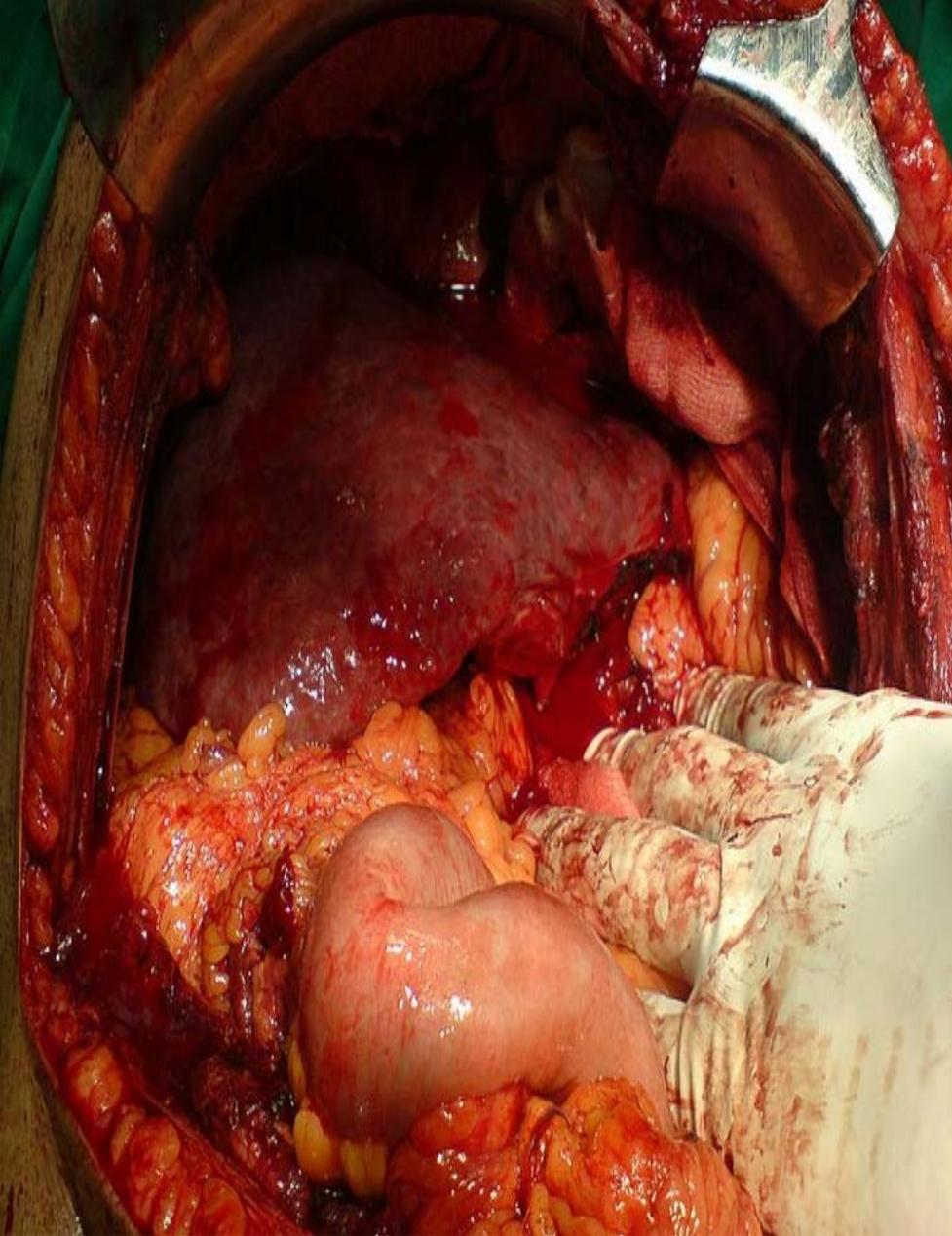
# STENTS





# DRUG ELUTING BALLOONS AND STENTS





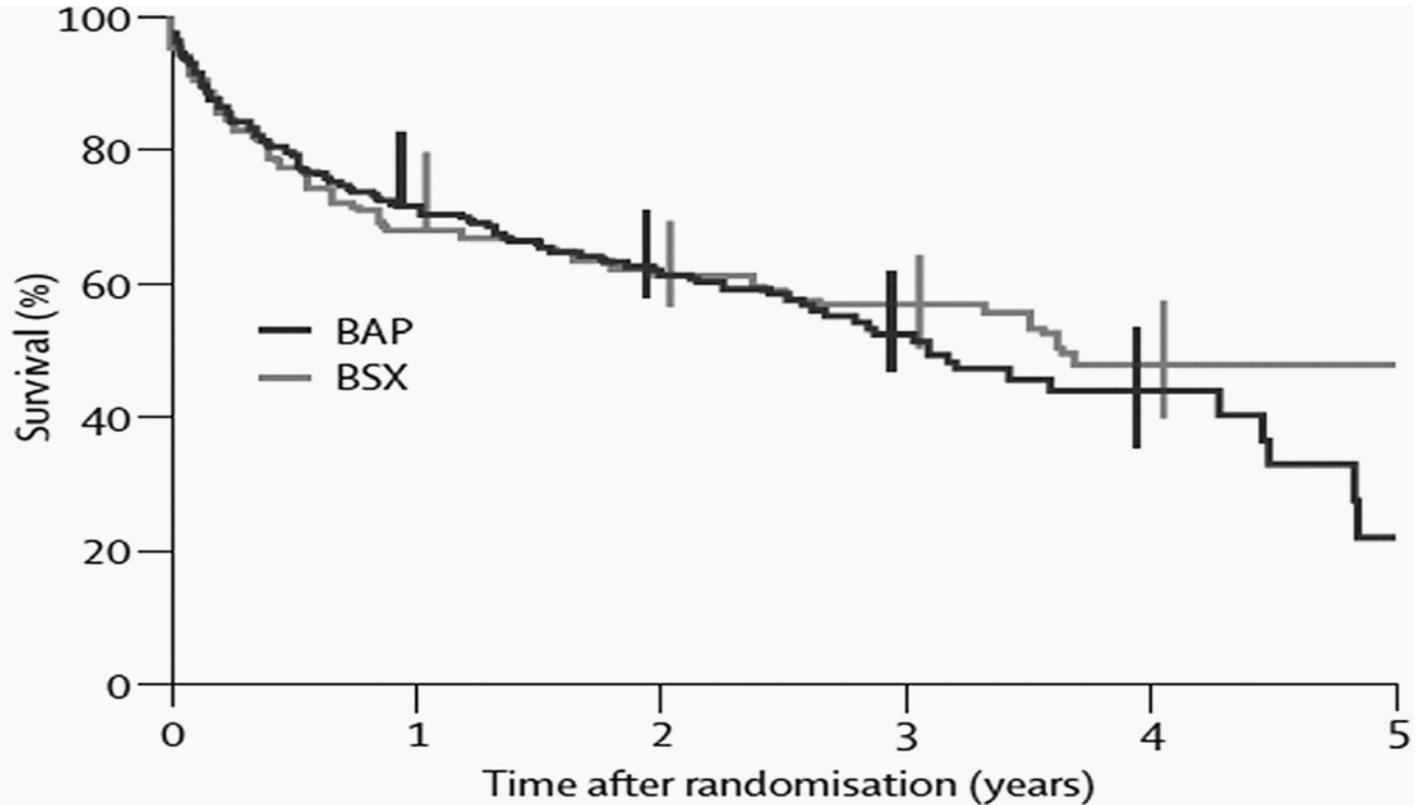
# **BASIL Trial: Bypass vs Angioplasty** **in Severe Ischemia of the Limb**

- Only RCT to date: surgery-first vs angioplasty-first for limb threatening ischemia (1999-2004)
- 452 patients with ischemia; 27 centers in UK
- Patients pre-selected as candidates for both PTA and surgery ; 29% of all-comers on audit
  - 34% deemed “unreconstructable”
  - 70% with ankle pressure >50 mm Hg
  - 42% diabetics
- Primary endpoint: amputation free survival
- Secondary endpoints: survival, M&M, LOS, cost, QOL.

Adam DJ et al. Lancet 2005; 366:1925-34.

Bradbury AW et al. J Vasc Surg 2010; 51 (Supplement S)

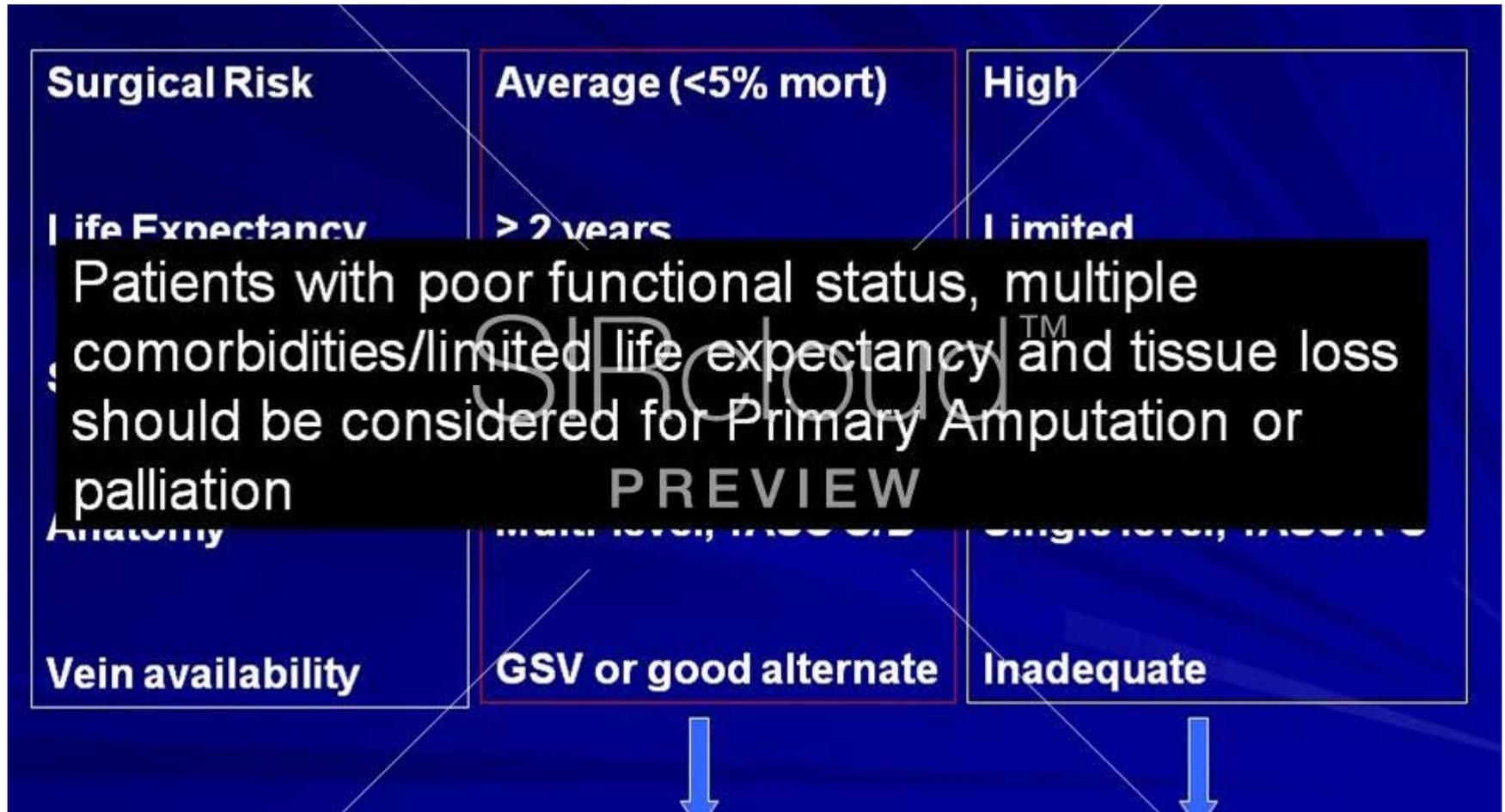
# CRITICAL ISCHAEMIA



## Number at risk

Angioplasty	224	149	100	51	19	2
Surgery	228	148	108	64	23	7

# PRIMARY AMPUTATION



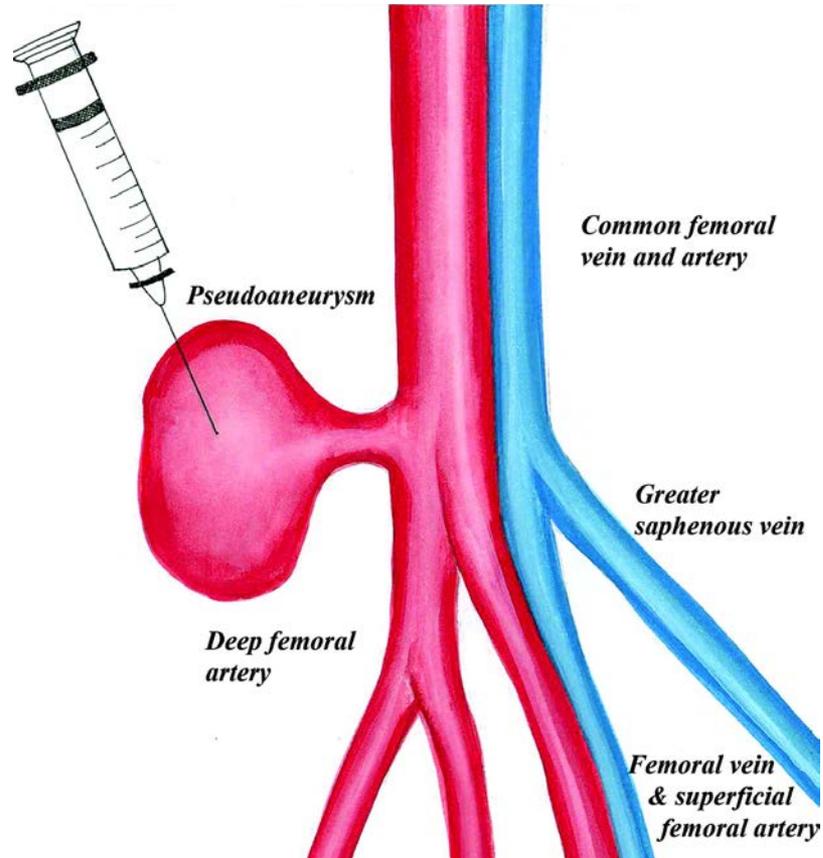
# WOUND MANAGEMENT



# FOOTWEAR AND ORTHOSIS



# COMPLICATIONS



# CASE 1

- 56 year old male
- 100m calf claudication
- Affecting QOL
- Only femoral pulse palpable

# History

- Rest pain
- What stops them from walking
- Smoking
- Medications
- Co-morbidities

# Examination

- Tissue loss/  
gangrene
- AAA

# INVESTIGATIONS

- LIPID SCREEN
- ABPI
- EXCLUDE DIABETES

# MANAGEMENT

- CLOPIDOGREL
- STATIN
- ACE INHIBITOR
- SUPERVISED EXERCISE PROGRAMME
- SMOKING CESSATION
- SURVEILLANCE









# CONCLUSIONS

- PATIENTS WITH PAD ARE HIGH RISK OF CV MORBIDITY AND MORTALITY
- MEDICAL MANAGEMENT OF CVS IS IMPORTANT
- MOST CLAUDICANTS WILL NOT LOSE THEIR LEG
- SYMPTOM CONTROL IN CLAUDICANTS STARTS WITH SUPERVISED EXERCISE
- REVASCULARISATION IN CLAUDICANTS HAS TO BE WEIGHED UP AGAINST RISKS OF INTERVENTION
- PATIENTS WITH REST PAIN/ ISCHAEMIC ULCERS / DRY GANGRENE SHOULD BE REFERRED TO VASCULAR SURGERY URGENTLY.
- PATIENTS WITH SIGNS OF SEPSIS SHOULD BE REFERRED IMMEDIATELY TO VASCULAR SURGERY