2022 MID-ATLANTIC CONFERENCE

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VASCULAR THERAPIES

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Sentara Vascular Specialists

Defining the Critical Limb Epidemic

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Disclosures

- Becton Dickinson – consultant and speaker
- Medtronic - speaker

Outline

- Defining Critical Limb Threatening Ischemia
- Defining Epidemic
- Socioeconomic impact
- Populations most effected
- Trajectory of the epidemic

Common Symptoms- Lower Extremities

Asymptomatic

- Nearly everyone who has PAD—even those who do not have leg symptoms—suffers from an inability to walk as fast, or as far, as they could before PAD.

Claudication

- Lower extremity symptoms confined to the muscles with a consistent (reproducible) onset with exercise and relief with rest.

Critical limb ischemia

- Ischemic rest pain, ulceration, or gangrene.

What and who?

- Critical limb ischemia vs Chronic limb-threatening ischemia
- 8-10M Americans have PAD
  - 500–1,000 new cases of CLTI per million people per year
- Prevalence CLTI - 12% in the adult population
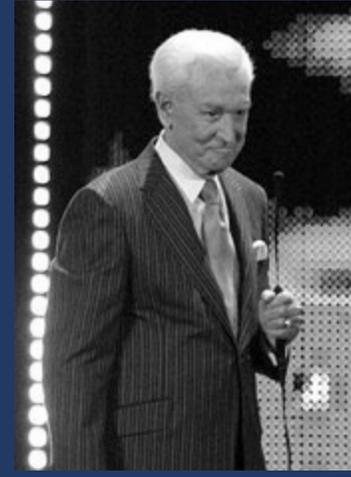
What do these people have in common?

Waylon Jennings

Ella Fitzgerald

Zsa Zsa Gabor

Bob Barker

All these famous people suffered from Peripheral Artery Disease.

It is estimated that PAD effects more than 8-12 million people in the US, many of which never get diagnosed or treated.

PAD is more prevalent and deadlier than many leading diseases

The prevalence of PAD is 12%[2]

- 8.5 million persons in the United States have PAD[1]
  - Affects 1 in 3 people older than over age 50 with diabetes
  - Only 25% are undergoing treatment
  - 40% do not complain of leg pain

- The 5 year mortality rate of PAD is 33%[3]

Diabetes	Coronary Heart Disease	PAD	Cancer	Stroke	Alzheimers
25.6	16.8	12	11.4	6.5	5.4
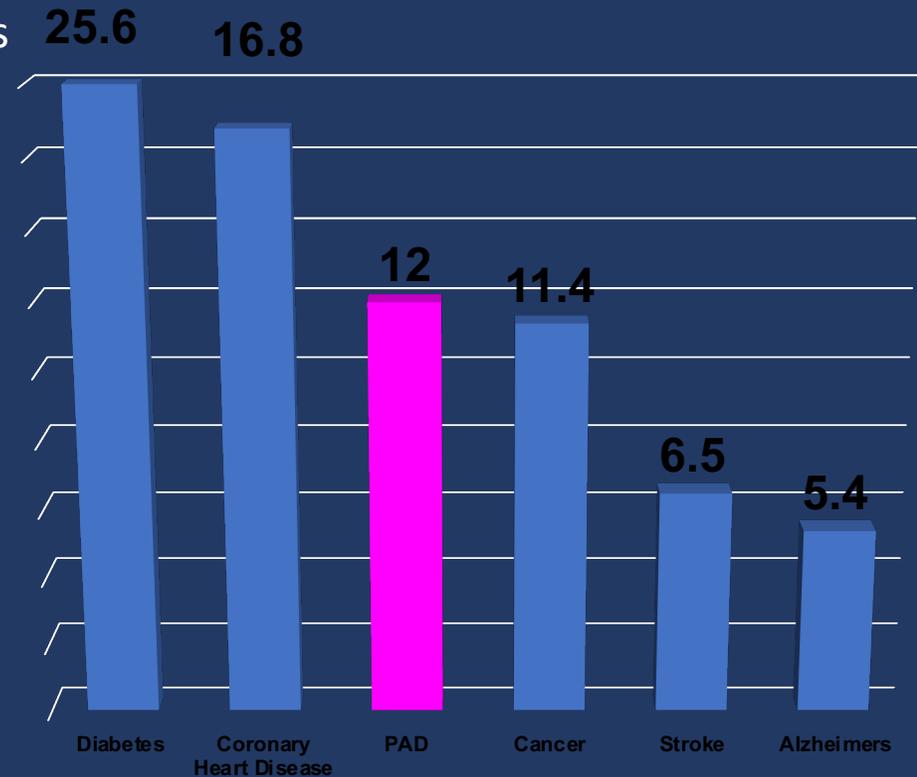
1. Go, A.S., AHA Statistical Update, Circulation. 2013; 127-e6-e245
2. Olin JW, et al. Journal for Vascular Surgery. Vol 52:6; 1616-1652..
3. Tomson, Joseph; Lip, Gregory Y H, Peripheral arterial disease: a high risk but neglected disease ....population, BMC Cardiovascular Disorders, ISBN: 14712261, 2005, Vol (Iss) Pgs: 5 (1) p.15

Causes and Risk Factors for PAD

- Age >50
- Smoking - 2-10x increase risk of PAD
- Hypertension - 2x increase risk of PAD
- Diabetes Mellitus - 3-4x risk of PAD
- High Cholesterol
- Abdominal Obesity
- Family History of CAD or PAD
- Kidney disease

"Peripheral Artery Disease." ClevelandClinic. Web. Dec 2015.
"Peripheral Arterial Disease (PAD) Fact Sheet". CDC. Web. 16 Jun 2016.
"Peripheral Arterial Disease (PAD)". American Diabetes Association (ADA). Web. 24 Sep 2014.
"Peripheral Arterial Disease (PAD)". Society of Interventional Radiology (SIR). Web. Jul 2016.
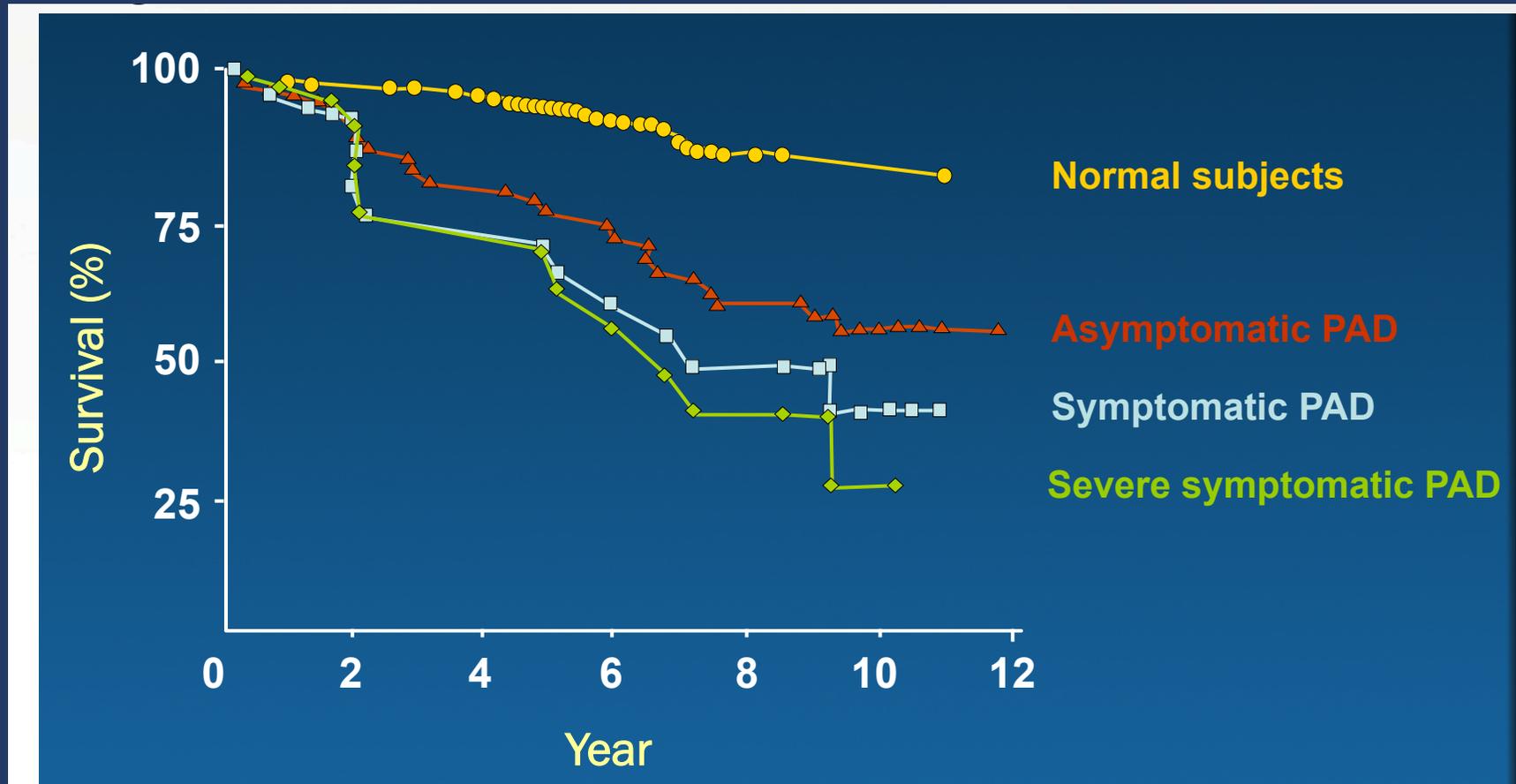
Who Should be Screened for PAD?

Based on the epidemiologic evidence, an "at risk" population for PAD can be objectively defined by:

- Aged less than 50 years with diabetes, and one additional risk factor (e.g., smoking, dyslipidemia, hypertension)

- Age 50–69 years, with a history of smoking or diabetes

- Age 70 years and older

- Walking impairment or claudication, ischemic rest pain, or lower extremity non-healing wounds

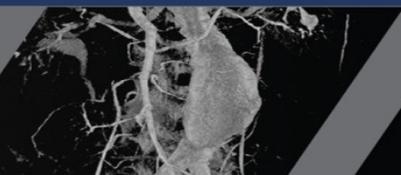- Known atherosclerotic coronary, carotid, or renal artery disease

Olin JW, et al. Journal for Vascular Surgery. Vol 52:6; 1616-1652..

Long-Term Survival in Patients With PAD

Normal subjects

Asymptomatic PAD

Symptomatic PAD

Severe symptomatic PAD

Patient Survival by Ankle-Brachial Index in Cardiovascular Health Study

Newman et al ATVB 1999;19; 538-545
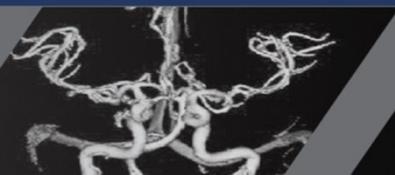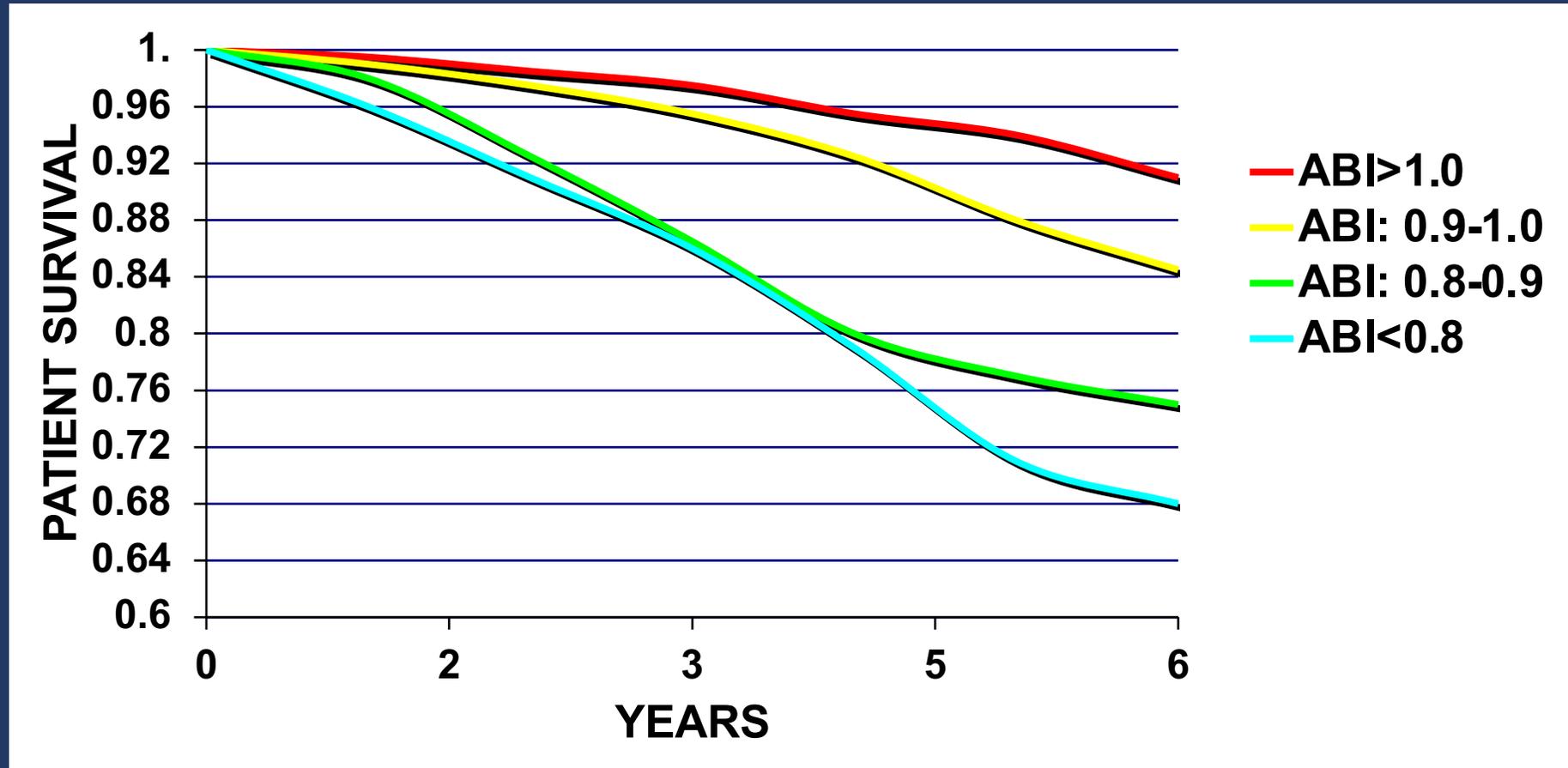
Relative 5-Year Mortality Rates
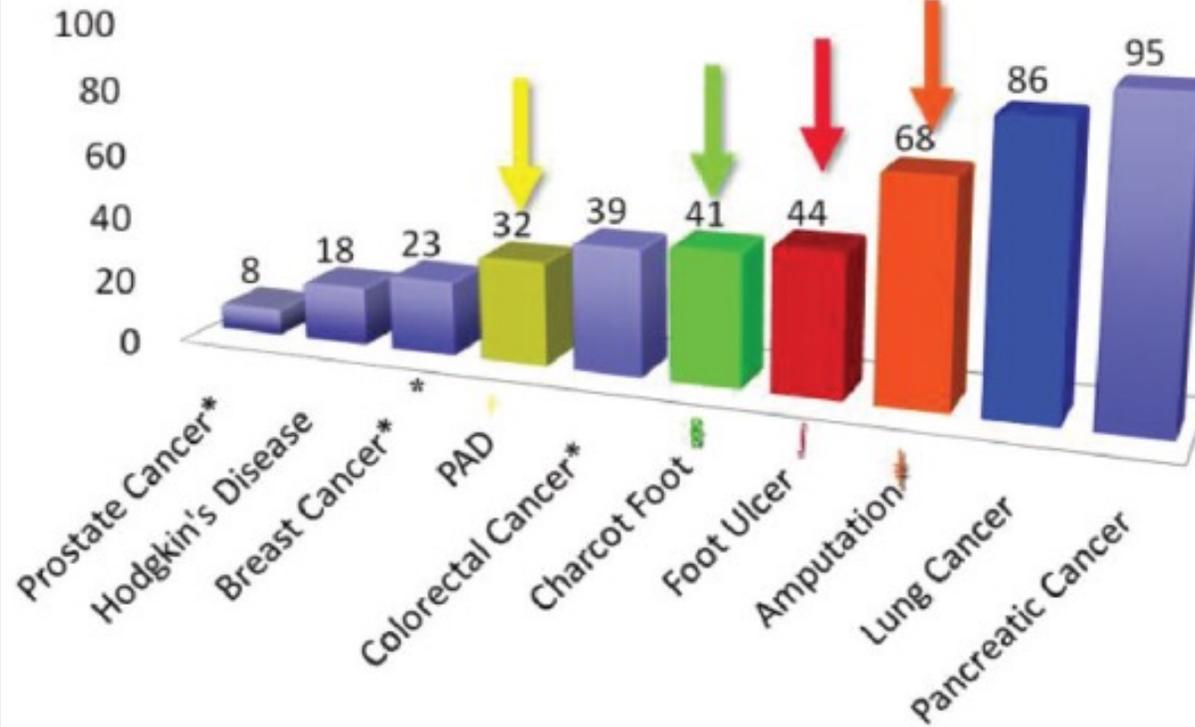
American Cancer Society. Cancer Facts and Figures, 2000.

†Criqui MH *et al*. N Engl J Med. 1992;326:381-6.

‡Larssen, Apelqvist *et al*: 1998

∫ Moulik *et al*: 2003

§ Van Baal *et al* 2010

Belch *et al*: Arch Int Med 2003; 163:884-892

PAD Awareness

A National PAD Public Awareness Survey found that the public is poorly informed about PAD.

From a cross-sectional, population-based telephone survey of 2,501 adults, over the age of 50:

26% Reported awareness of PAD

19% Percentage of those who were "PAD aware", and received their PAD information from healthcare professionals

25% Percentage of those who were "PAD aware," and who knew PAD is associated with increased risk of heart attack and stroke

Awareness tended to be lowest among those who were older, male, non-white and had a lower education or income level

Hirsch AT, et al. Circulation. 2007;116;2086-2094.

Classification of PAD

Rutherford Stage	Clinical Symptoms	Fontaine Stage	Clinical Symptoms
0	Asymptomatic	I	Asymptomatic
1	Mild Claudication	II	Intermittent Claudication
2	Moderate Claudication	IIa	Pain walking more than 200 m
3	Severe Claudication	IIb	Pain walking less than 200 m
4	Rest Pain	III	Rest pain
5	Minor Tissue Loss	IV	Necrosis and gangrene
6	Mayor Tissue Loss	-	-

Risk stratification based on Wound, Ischemia, and foot Infection (WIfI)

Wound
0: No Ulcer and No Gangrene
1: Small Ulcer and No Gangrene
2: Deep Ulcer and Gangrene limited to toes
3: Extensive Ulcer or Extensive Gangrene

Ischemia
Toe Pressure / $tcpO_2$

0: > 60 mmHg
1: 40-59
2: 30-39
3: < 30

Foot infection
0: Noninfected
1: Mild (< 2 cm cellulitis)
2: Moderate (> 2 cm cellulitis /purulence)
3: Severe (systematic response / sepsis)

Table IV. a and b, Risk/benefit: Clinical stages by expert consensus

a, Estimate risk of amputation at 1 year for each combination

	Ischemia – 0				Ischemia – 1				Ischemia – 2				Ischemia – 3			
W-0	VL	VL	L	M	VL	L	M	H	L	L	M	H	L	M	M	H
W-1	VL	VL	L	M	VL	L	M	H	L	M	H	H	M	M	H	H
W-2	L	L	M	H	M	M	H	H	M	H	H	H	H	H	H	H
W-3	M	M	H	H	H	H	H	H	H	H	H	H	H	H	H	H
	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3

b, Estimate likelihood of benefit of/requirement for revascularization (assuming infection can be controlled first)

	Ischemia – 0				Ischemia – 1				Ischemia – 2				Ischemia – 3			
W-0	VL	VL	VL	VL	VL	L	L	M	L	L	M	M	M	H	H	H
W-1	VL	VL	VL	VL	L	M	M	M	M	H	H	H	H	H	H	H
W-2	VL	VL	VL	VL	M	M	H	H	H	H	H	H	H	H	H	H
W-3	VL	VL	VL	VL	M	M	M	H	H	H	H	H	H	H	H	H
	f-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3

fI, foot Infection; I, Ischemia; W, Wound.

Premises:

1. Increase in wound class increases risk of amputation (based on PEDIS, UT, and other wound classification systems)
2. PAD and infection are synergistic (Eurodiale); infected wound + PAD increases likelihood revascularization will be needed to heal wound
3. Infection 3 category (systemic/metabolic instability): moderate to high-risk of amputation regardless of other factors (validated IDSA guidelines)

Four classes: for each box, group combination into one of these four classes

Very low = VL = clinical stage 1
Low = L = clinical stage 2
Moderate = M = clinical stage 3
High = H = clinical stage 4

Clinical stage 5 would signify an unsalvageable foot

Table VI. Clinical stages (major limb amputation risk) based on Wound, Ischemia, and foot Infection (WIfI) classification

Risk of amputation	Proposed clinical stages	WIfI spectrum score
Very low	Stage 1	W0 I0 fI0,1
		W0 I1 fI0
		W1 I0 fI0,1
		W1 I1 fI 0
Low	Stage 2	W0 I0 fI2
		W0 I1 fI1
		W0 I2 fI0,1
		Wo I3 fI0
		W1 I0 fI2
		W1 I1 fI1
		W1 I2 fI0
		W2 I0 fI0/1
		W0 I0 fI3
		W0 I2 fI1,2
		W0 I3 fI1,2
		W1 I0 fI3
		W1 I1 fI2
		W1 I2 fI1
		W1 I3 fI0,1
		W2 I0 fI2
Moderate	Stage 3	W2 I 1 fI0,1
		W2 I2 fI0
		W3 I0 fI0,1
		W0 I1,2,3 fI3
		W1 I1 fI3
		W1 I2,3 fI2,3
		W2 I0 fI3
		W2 I1 fI2,3
		W2 I2 fI1,2,3
High	Stage 4	W2 I3 fI0,1,2,3
		W3 I0 fI2,3
		W3 I1,2,3 fI0,1,2,3

Clinical stage 5 would signify an unsalvageable foot (most often because of wound extent or severity of infection).

Why WIFi?

Society for Vascular Surgery (SVS) WIfI Classification Identifies Patients Most Likely To Benefit From

Multicenter study of chronic limb-threatening ischemia (CLTI) of 1654 limbs and 169 amputations

Scores based on WIfI (Wound, Ischemia and foot Infection) clustered into quartiles

Risk difference quartiles

Q1 – Highest benefit

Q2 – Moderate benefit

Q3- Low benefit

Q4 – Questionable benefit

Observed Amputation Rate

Q1 → 4.4%

Q2 → 14.8%

Q3 → 28.1%

Q4 → 51.2%

The SVS WIfI score identifies which CLTI patients will have the greatest and the least benefit from revascularization.

Mayor et al. *J Vasc Surg September 2019*
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- 1% to 3% of Claudicants ever require a major amputation over a 5-year period
- Smoking is the most important risk factor for the progression of local disease in the legs, with an amputation rate 11 times greater in smokers than nonsmokers
- **2% to 4% of claudicants have a nonfatal cardiovascular event every year – marker for disease**
- Average claudicant is more likely to have a nonfatal myocardial infarction (MI) or stroke in the next year that of ever requiring a major amputation for his leg ischemia.
- The mortality in claudicants is 2.5x baseline with 30% at 5 years, 50% at 10 years, and 70% at 15 years.

CLTI is not

- Purely venous ulcers
- Acute limb ischemia
- Acute trash foot
- Ischemia due to emboli, acute trauma
- Mangled extremity
- Nonatherosclerotic conditions
  - Vasculitides
  - collagen vascular disease
  - Buerger's disease
  - neoplastic disease
  - Dermatoses
  - radiation arteritis.

Epidemiology

- The PARTNERS (PAD Awareness, Risk, and Treatment: New Resources for Survival)
  - CLTI present in 29% of the patients aged 50+ with at least a 10-pack-per-year history of smoking or a history of diabetes
  - Greater than 70% of primary care providers in the PARTNERS study were unaware of the presence of CLTI in their patients who had the disease
- The Reduction of Atherothrombosis for Continued Health (REACH) registry
  - 1/6 patients PAD, CVD , or CAD had involvement of one or two other arterial beds.
  - Identified a substantial gap between recommended clinical guidelines and actual clinical practices in caring for patients with or at risk for atherothrombosis

Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral Arterial Disease Detection, Awareness, and Treatment in Primary Care. *JAMA.* 2001;286(11):1317–1324. doi:10.1001/jama.286.11.1317

Ohman EM, Bhatt DL, Steg PG, Goto S, Hirsch AT, Liau CS, Mas JL, Richard AJ, Röther J, Wilson PW; REACH Registry Investigators. The REduction of Atherothrombosis for Continued Health (REACH) Registry: an international, prospective, observational investigation in subjects at risk for atherothrombotic events-study design. Am Heart J. 2006 Apr;151(4):786.e1-10. doi: 10.1016/j.ahj.2005.11.004. PMID: 16569533.
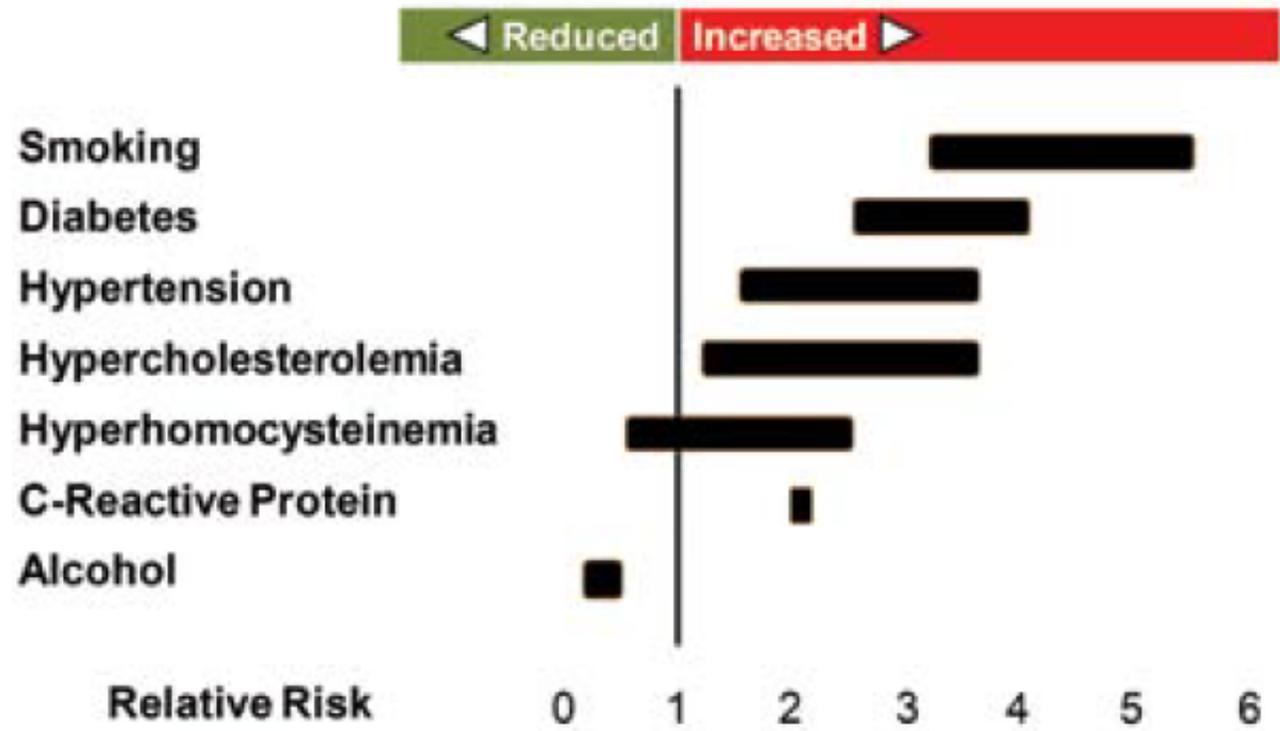
Figure 2. The relative importance of key risk factors in the progression of peripheral arterial disease.

# Relationship Between PAD & Coronary Artery Disease (CAD)

PAD is closely related to CAD

Atherosclerosis is the primary underlying cause of vascular disease; accounts for 90% of PAD cases[1]

60-80% of lower extremity PAD patients have significant CAD in at least one coronary artery[1]

40-60% of patients with PAD have coronary & cerebral artery disease[1]

21% of patients with PAD will have MI, stroke, cardiovascular death or hospitalization within one year, compared to 15% of patients with established coronary artery disease or prior heart attack[2]
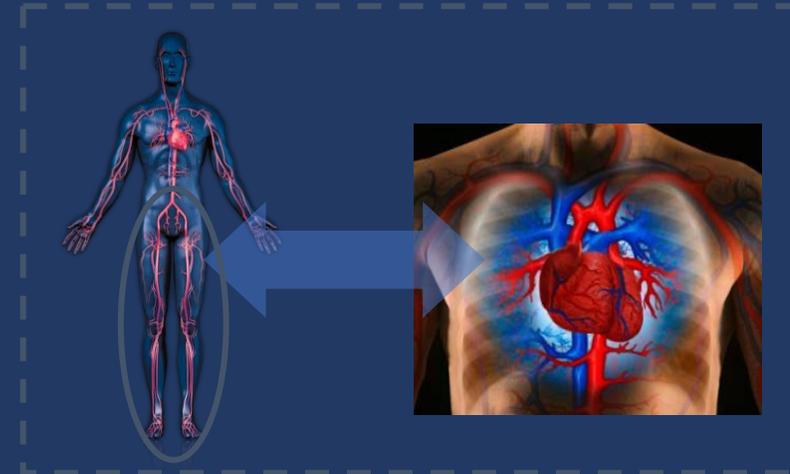
1. Norgren, L.et al. .Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). 2007.
2. Cacoub, et al. REACH Registry. Atherosclerosis 2006
Illustrations included are artist's renditions, not drawn to scale

Impact of PAD on Patients

The consequences of PAD are two-fold: decrease in quality of life and an increase in related cardiovascular events.

Decrease in Quality of Life

Intermittent claudication
Atypical leg pain
Sedentary lifestyle
Depression
Amputation

Cardiovascular Morbidity and Mortality

Risk of angina is
2-3 times higher than
age-matched population
2-3% annual incidence
of non-fatal MI
CAD is the most common
cause of death in patients
with PAD (40-60%)

Olin JW, et al. Journal for Vascular Surgery. Vol 52:6; 1616-1652.
Hirsch AT, et al. Circulation. 2006. 113: 463-654.

Potential Components and Required Specialists for the Diagnosis and Treatment of Critical Limb Ischemia

Potential components of critical limb ischemia diagnosis, management, and follow-up
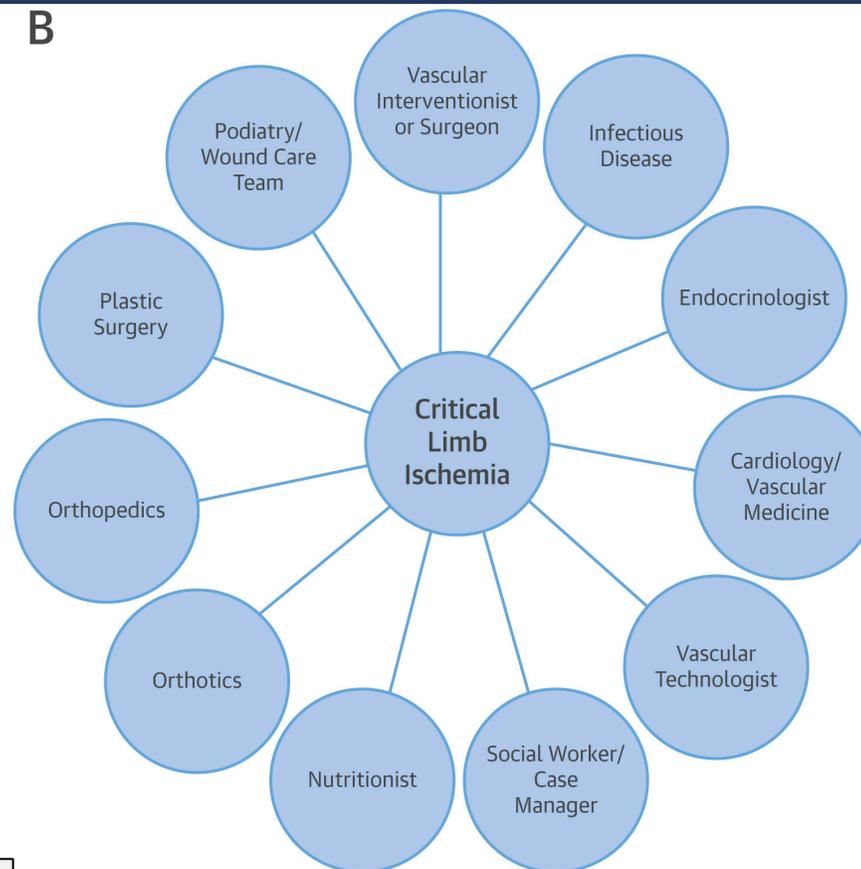
Multidisciplinary team of experts that may be required to address these factors.

Conclusion

- The USA and world are experiencing an epidemic of CLTI
- Medical management is integral for early detection and management
- A multidisciplinary committee may improve outcomes in the difficult to treat popluation