Women & Peripheral Arterial Disease

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Interventional Cardiology
November 15th, 2019

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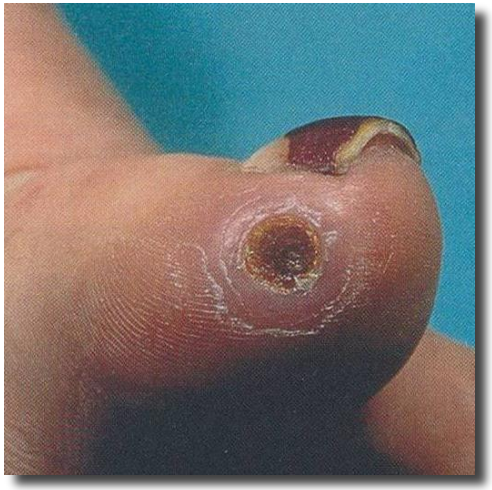
Presenter	**Disclosure**
Georges Nseir, MD	None

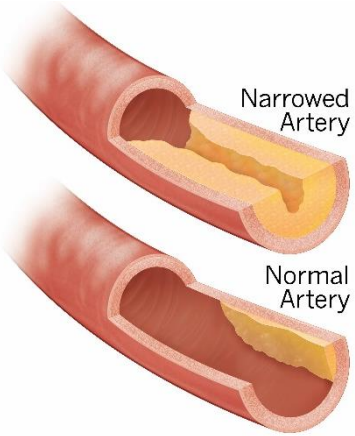
PAD: Peripheral Arterial Occlusive Disease



The problem: peripheral arterial disease

PAD affects 8-12 million people in the U.S.[1]

150,000 Amputations Yearly Due to CLI[2]

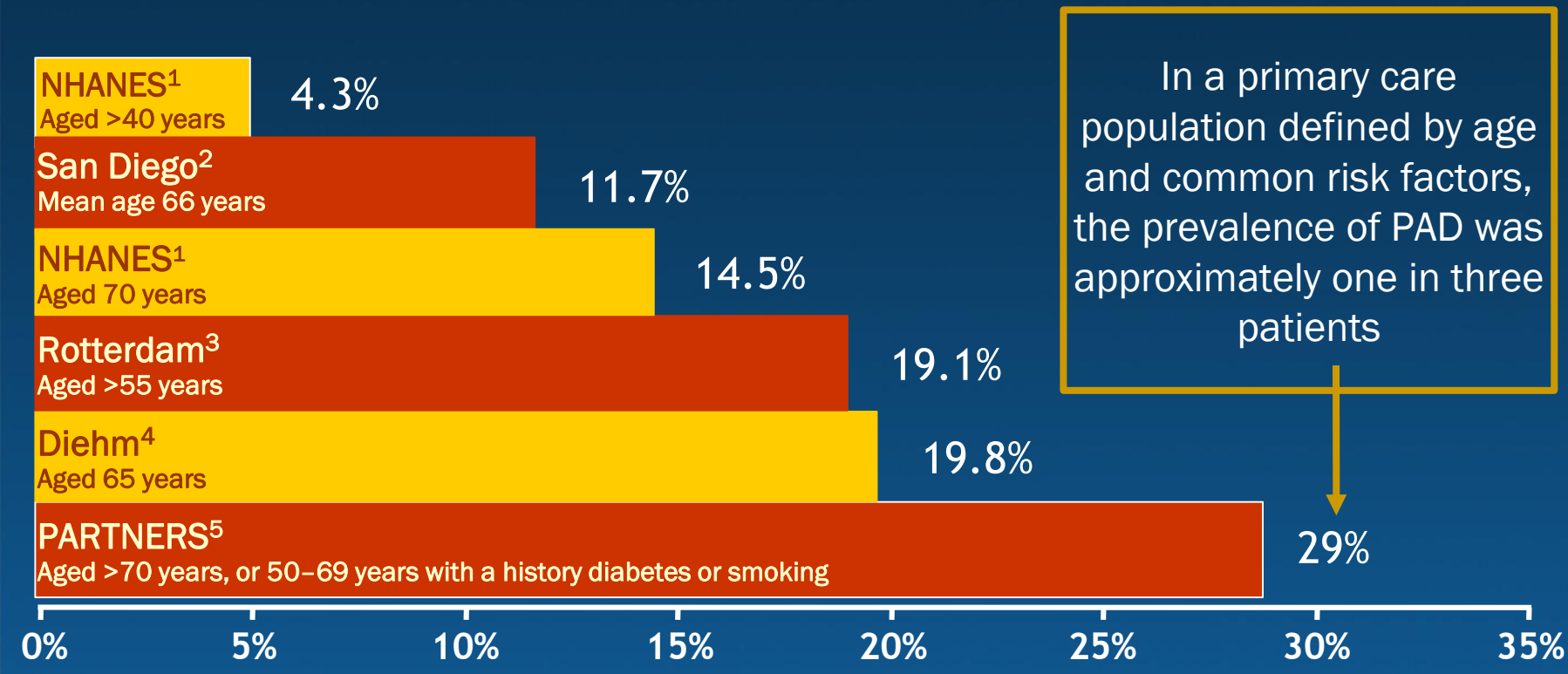


Up to 2 Million with Critical Limb Ischemia (CLI)[2]

1. US Department of Health & Human Services National Institute of Health August 2006.
2. Jaff, MR, Biamino G; "Conquering Critical Limb Ischemia" ;Endovascular Today, February 2004, Volume 3, No. 2

Images provided by CSI.

Prevalence of PAD



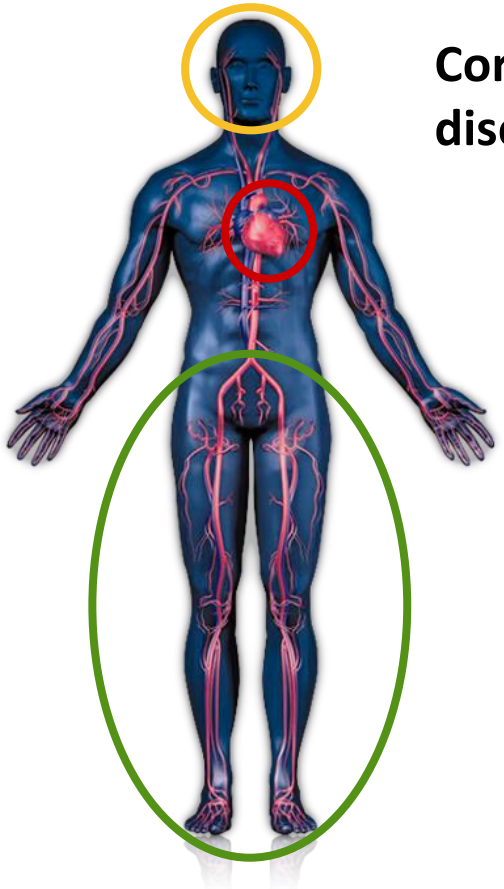
NHANES=National Health and Nutrition Examination Study;

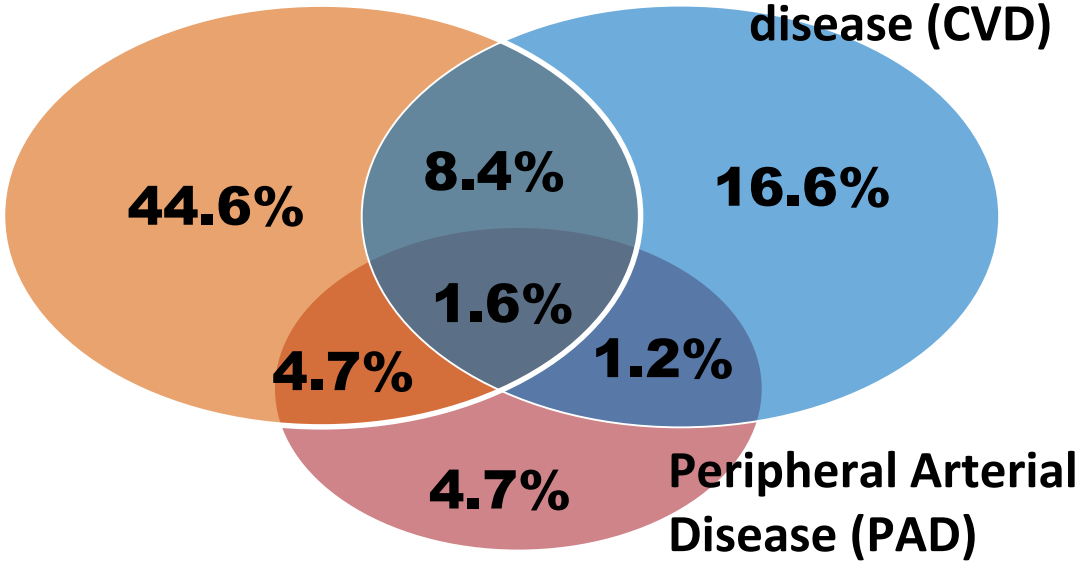
PARTNERS=PAD Awareness, Risk, and Treatment: New Resources for Survival [program].

1. Selvin E, Erlinger TP. Circulation. 2004;110:738-743.
2. Criqui MH et al. Circulation. 1985;71:510-515.
3. Diehm C et al. Atherosclerosis. 2004;172:95-105.
4. Meijer WT et al. Arterioscler Thromb Vasc Biol. 1998;18:185-192.
5. Hirsch AT et al. JAMA. 2001;286:1317-1324.

Relationship Between PAD, Cerebral Artery Disease, and Coronary Artery Disease (CAD)

Because atherosclerosis is the primary underlying cause of vascular artery disease, it is very common for patients to have multiple forms of arterial disease





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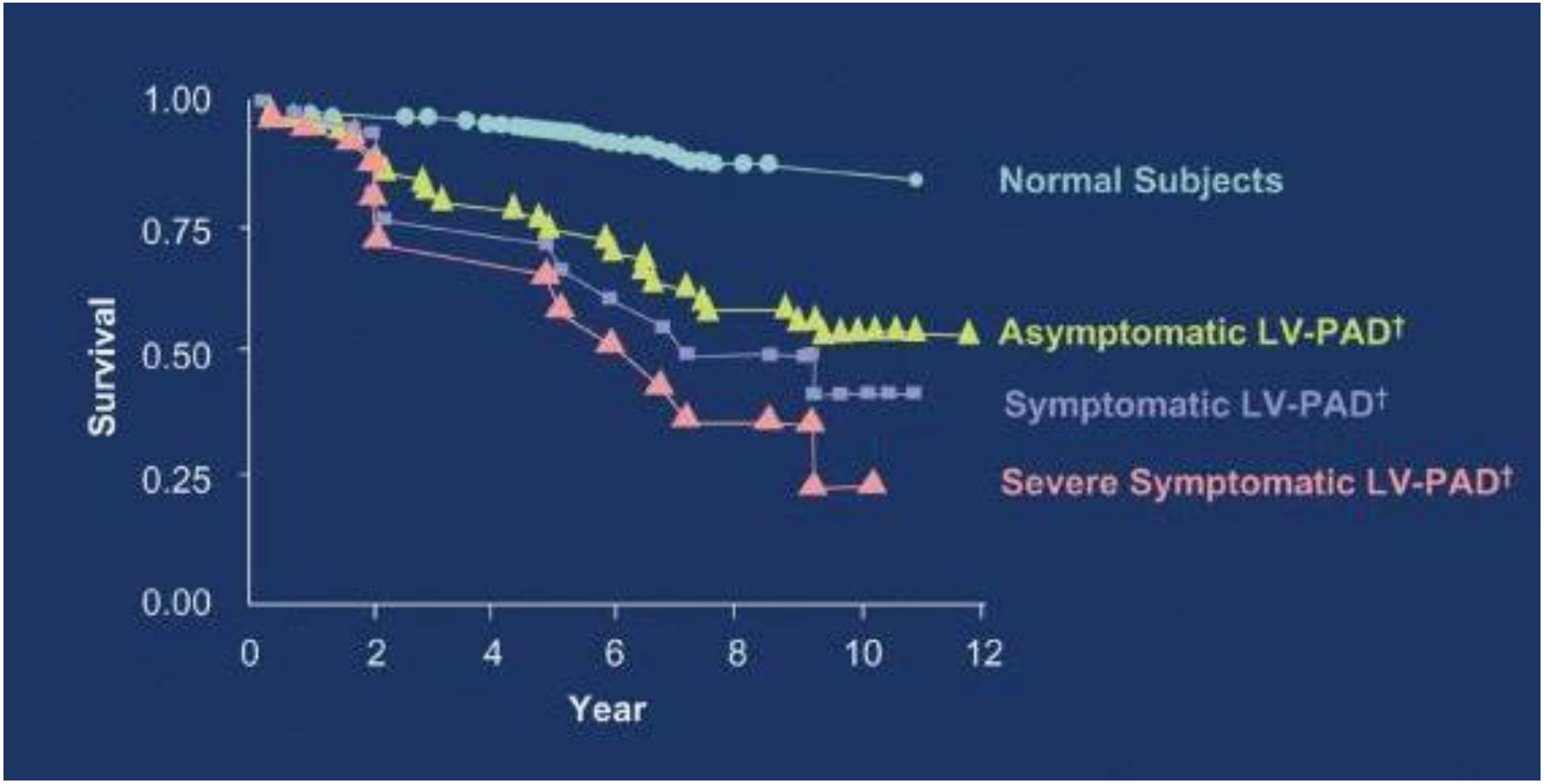
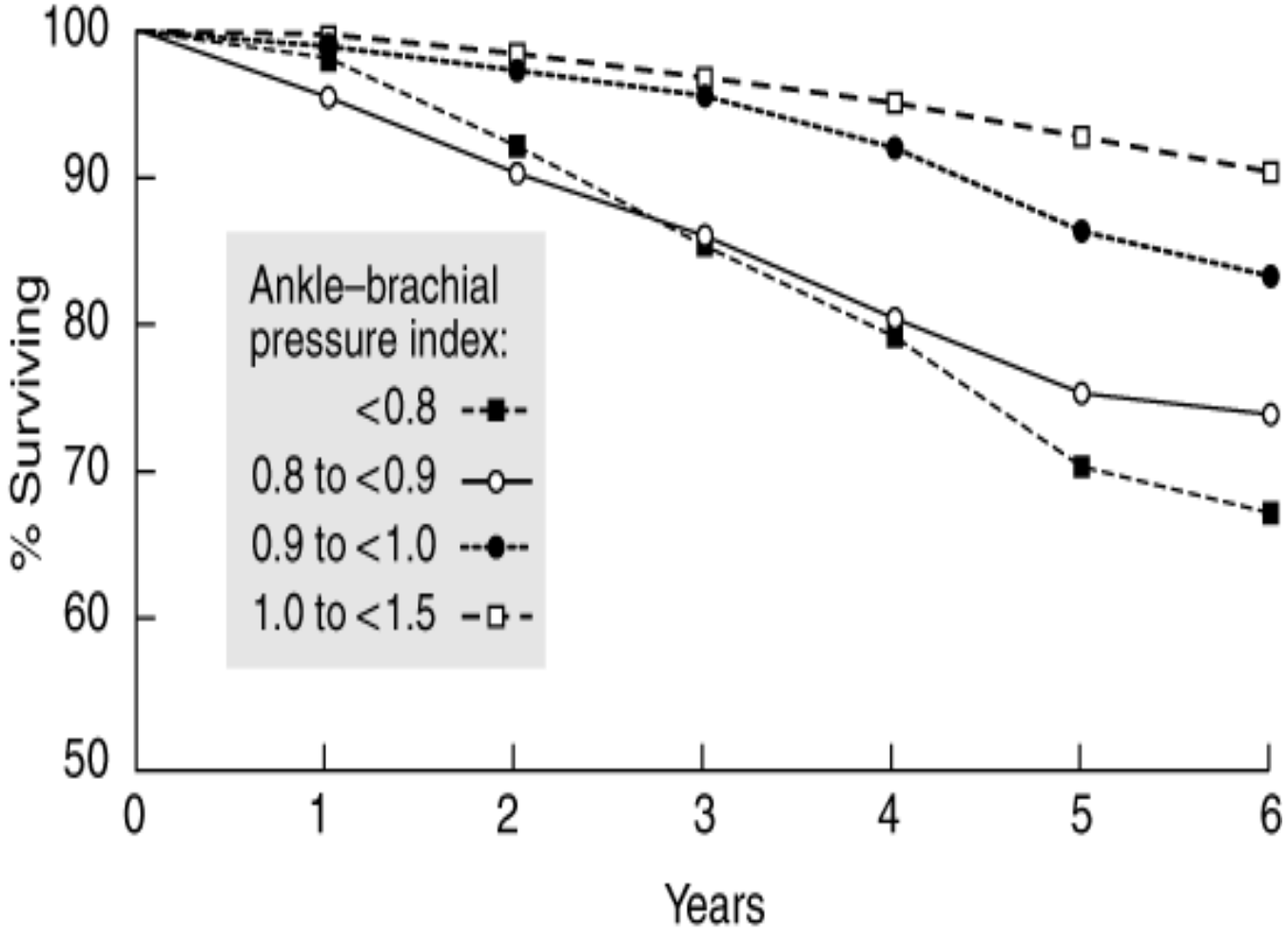
[1]Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II) p. 22 2004.

PAD: LONG-TERM MORTALITY

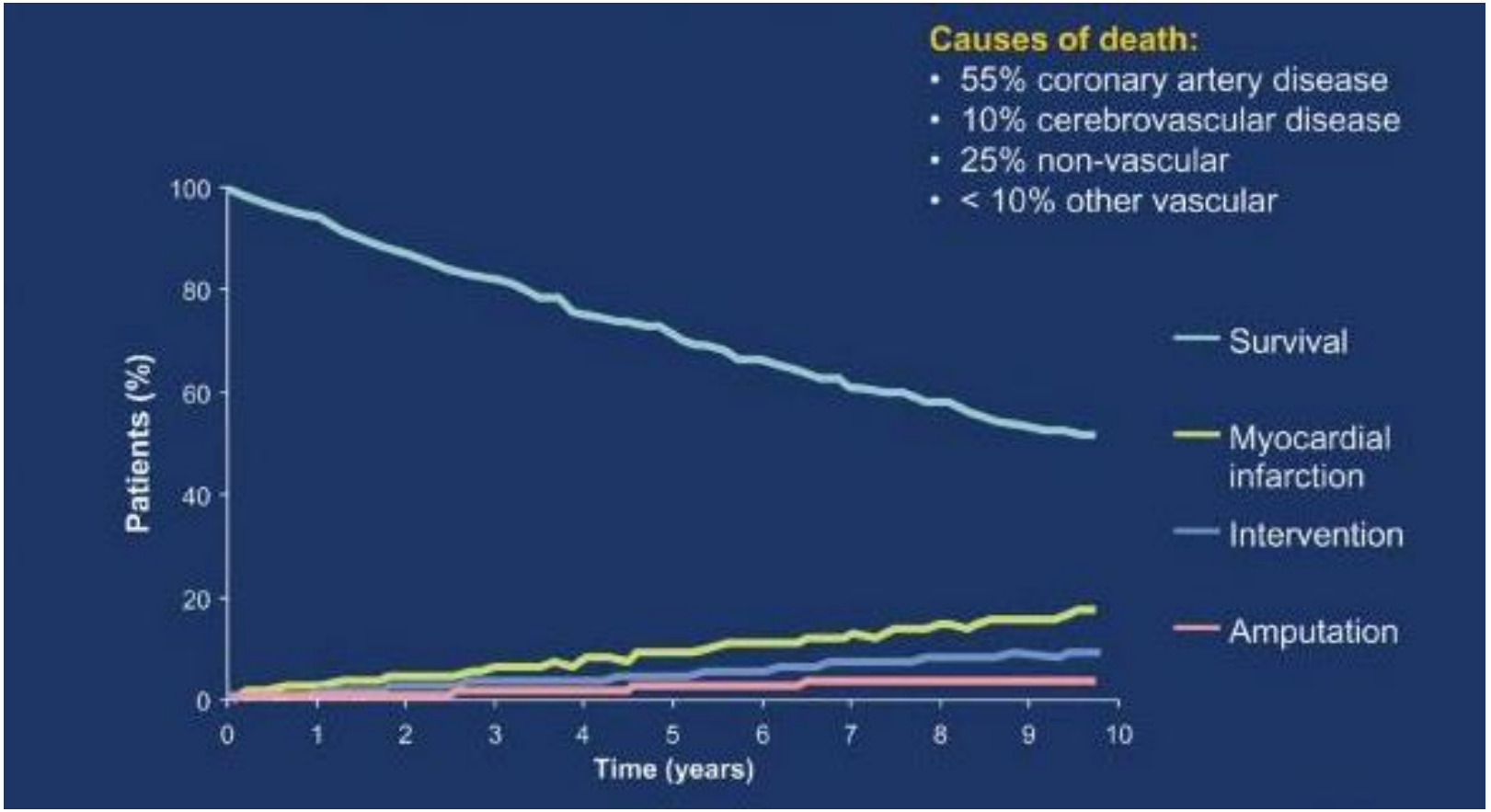


Criqui MH, et al, Vasc Med, 2001

PAD: ABI PREDICTS SURVIVAL



Claudication Long Term Outcome



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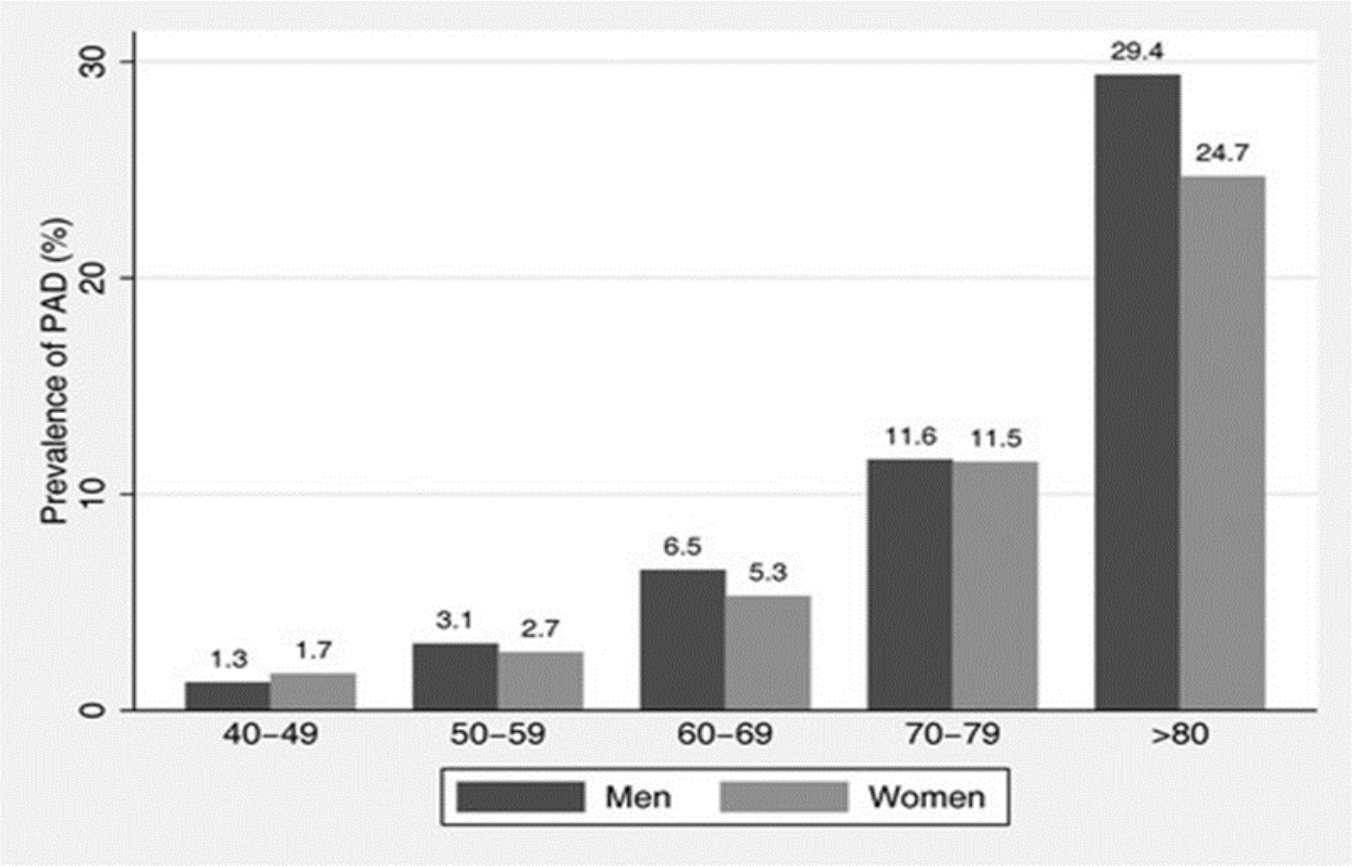
Ouriel K, Lancet, 2001

PREVALENCE vs Age



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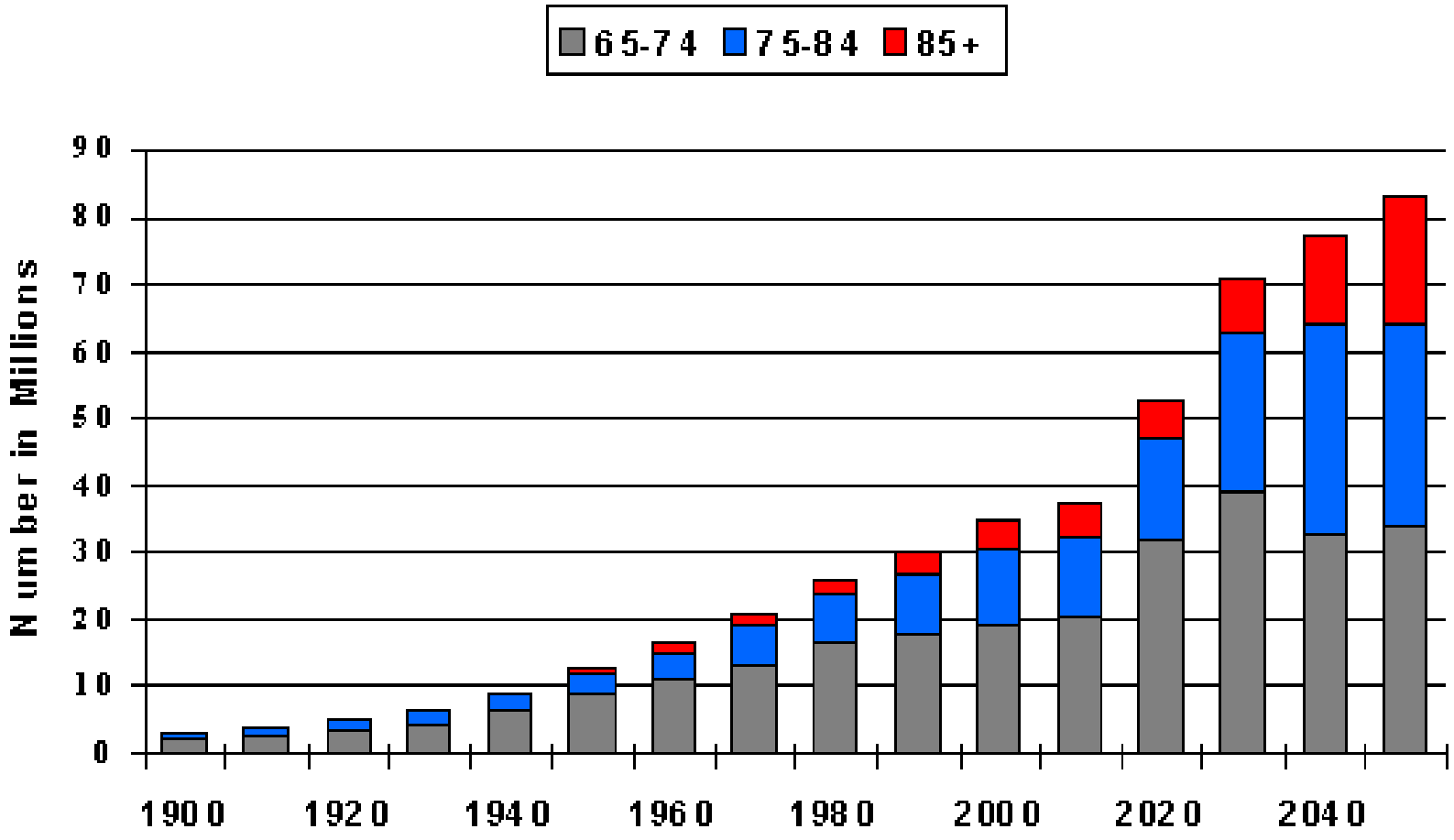
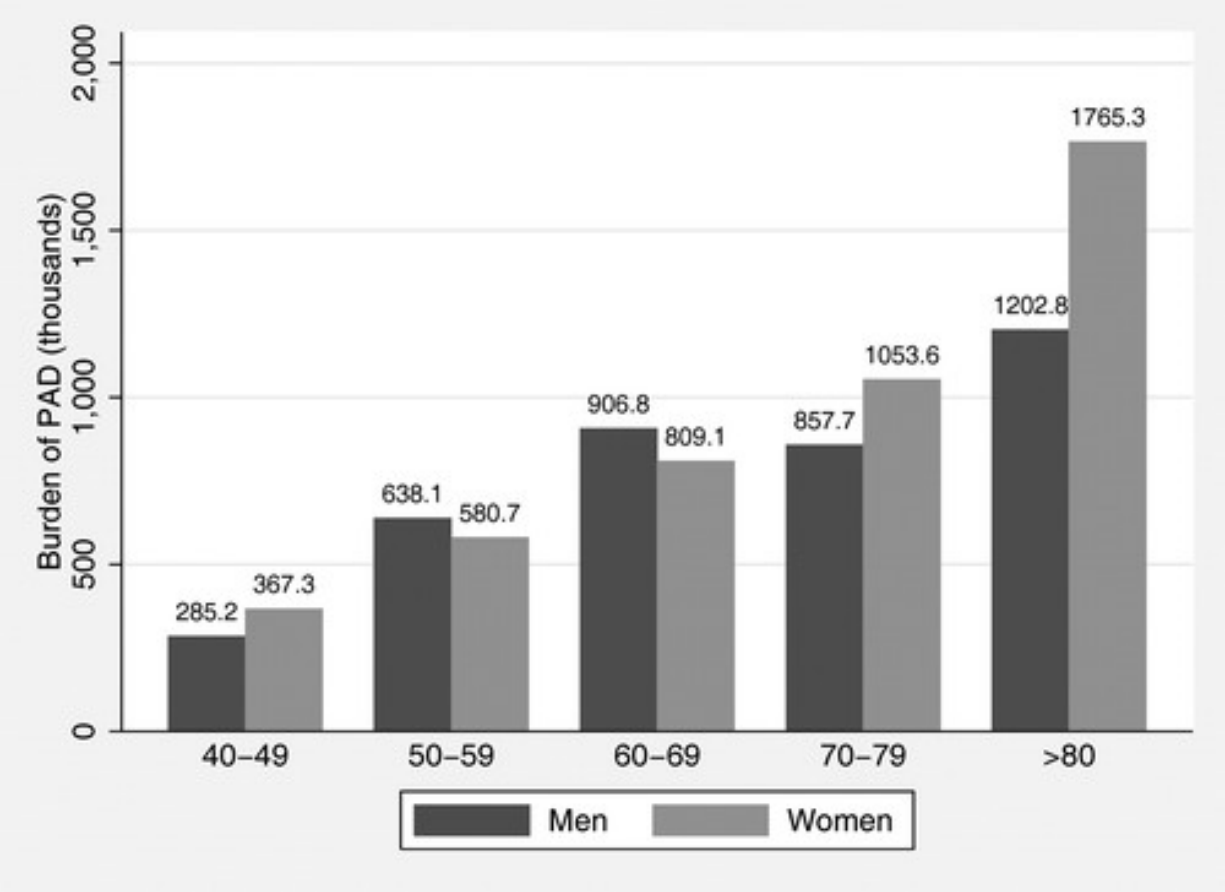
Alan T. Hirsch. Circulation. A Call to Action: Women and Peripheral Artery Disease, Volume: 125, Issue: 11, Pages: 1449-1472, DOI: (10.1161/CIR.0b013e31824c39ba

Growth of U.S. Older Adult Population



Burden of the Disease



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PAD in Women:

Often Unrecognized and Untreated According to AHA

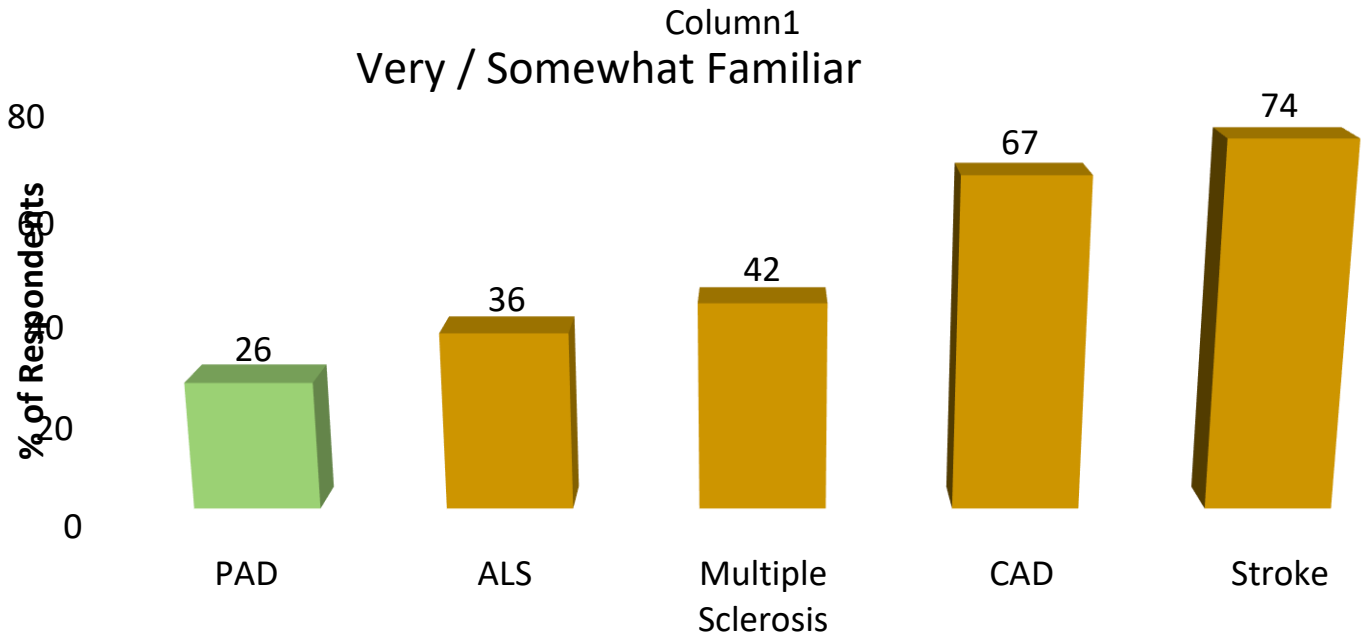
American Heart Association scientific statement - February 15, 2012

> Healthcare providers should proactively increase awareness of and test women at risk for PAD
>
> - The AHA, Vascular Disease Foundation and Peripheral Artery Disease Coalition

"Women with peripheral artery disease, or PAD, are two to three times more likely to have a stroke or heart attack than those without it — yet it's often unrecognized and untreated, especially in women"[1]

1. Peripheral artery disease undertreated, understudied in women. The American Heart Association Web site. http://newsroom.heart.org/news/peripheral-artery-disease-undertreated-228645. Accessed April 25, 2013.

Patient awareness of PAD is very low[1]



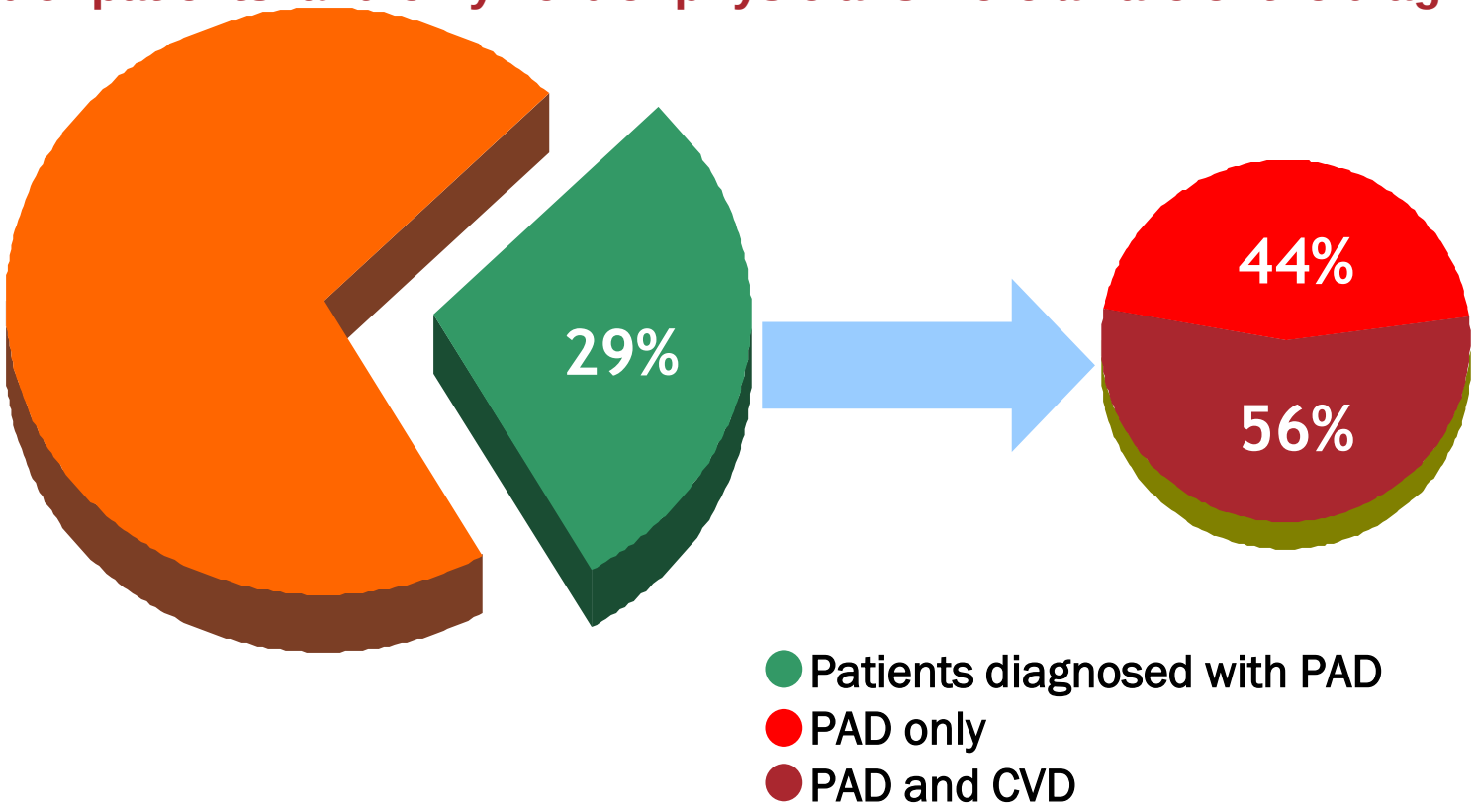
N = 2501 ≥ 50 years surveyed for awareness of PAD and other diseases

1. Hirsch AT, Murphy TP, Lovell MB, et al. Gaps in Public Knowledge of PAD: the First National PAD Public Awareness Survey. *Circulation*. 2007; 116:2086-2094.

PARTNERS: Prevalence of PAD and CVD in Primary Care Practices

29% of Patients Were Diagnosed With PAD Using ABI

83% of patients and only 49% of physicians were aware of the diagnosis



ABI=ankle-brachial index; CAD=coronary artery disease; CVD=cardiovascular disease.

Hirsch AT et al. *JAMA*. 2001;286:1317-1324.

PAD in Women

- A major knowledge gap exists.
  - Gender specific prevalence has been incompletely evaluated (versus CAD and Stroke)
  - Delayed Post-Menopausal presentation of PAD
  - Gender based distinction in clinical presentation
  - Sensitivity and specificity of PAD diagnostic tests unknown
  - Treatment : benefits and harm
    - Due to limited inclusion of women in trials.

Research Trials

Impact of Gender on PAD Treatment Outcomes

Type of Intervention	Randomized Studies, N	Total Participants, N	Primary Outcomes Measured	Studies Reporting Gender of Participants, n (%)	Female Participants, n (%)	Studies Reporting Gender-Specific Results, n (%)	Gender-Specific Results Reported
Supervised exercise	37	1814	PWT/D; COT/D; 6-min walk test	31 (86)	493 (27; Range 0–81)	1 (3)	Insufficient data
Cilostazol	Pooled analysis of 9 (6 published, 3 unpublished)	2251	PWT/D; COT/D	9 (100)	532 (24; Range 16–25)	None individually; pooled analysis of all studies	No gender-by-treatment interaction
Surgical revascularization	40	16 324	Patency, repeat operation, limb salvage, survival, amputation-free survival, adverse events, ABI, digital pressure, PWT/D, blood flow, QOL	34 (85)	4467 (Range 0–60)	12	No gender-by-treatment interaction (n = 6); decreased patency in women (n = 3); increased perioperative adverse events in women (n = 1); gender-race interaction with decreased patency in black women (n = 1); gender–graft diameter interaction effect on patency (n = 1)
Endovascular revascularization	22	2665	Patency, technical success, repeat intervention, limb salvage, amputation-free survival, recurrent ischemia, symptoms, adverse events, ABI, ankle pressure, biomarkers, QOL, functional outcomes, PWT/D, COT/D	19 (86)	847 (Range 20–50)		
Surgical and endovascular revascularization	7	1506	Patency, adverse events, survival, amputation-free survival, ABI	5 (71)	393 (Range 0–40)	None	None

Overall 20% Participation

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Predictors of PAD

- Four Main Risk Factors for PAD[1]

Hypertension	Smoking	Diabetes	High Cholesterol

More closely associated with PAD than Coronary Heart Disease (CHD)[1]

- 95% of PAD patients had at least 1 risk factor vs 80% of CHD patients
- 20-30% of patients with PAD have Diabetes
- Active smoking 2-3 times more strongly associated with PAD than CHD

Significantly and Independently Associated with Higher Risk of PAD[1]

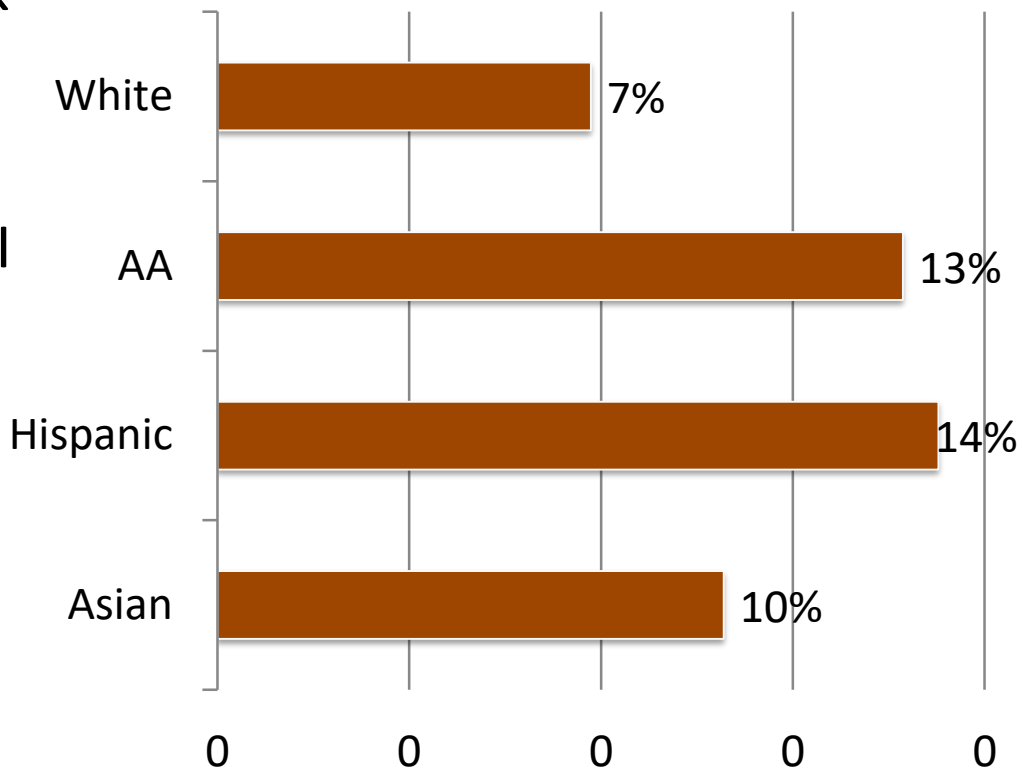
Healthcare Professionals Study, 44,985 subjects, 24 year follow-up

Women are Older
More Diabetes
More Hyperlipidemia
More Smokers

1. *Joosten MM, Pai JK, Bertoia ML, et al. Associations Between Conventional Cardiovascular Risk Factors and Risk of Peripheral Artery Disease in Men. JAMA* 2012;308(16):1660-1667

Diabetes Mellitus and Women

- Diabetes increase the risk of PAD 4x
- Increase mortality in patients with PAD and CLI
- Increase the risk of lower extremity amputation



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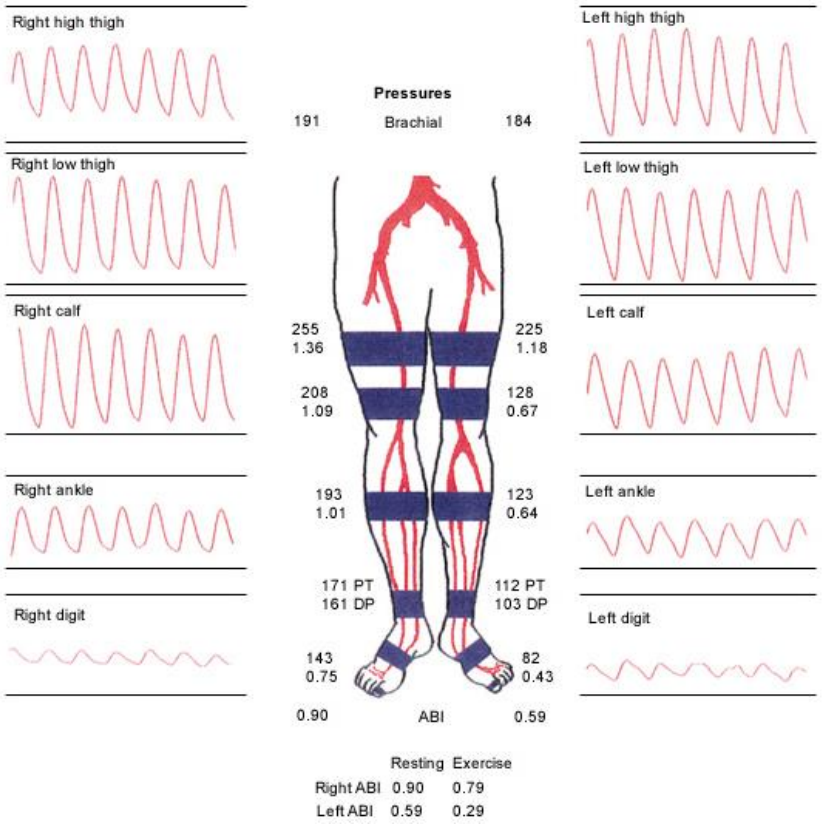
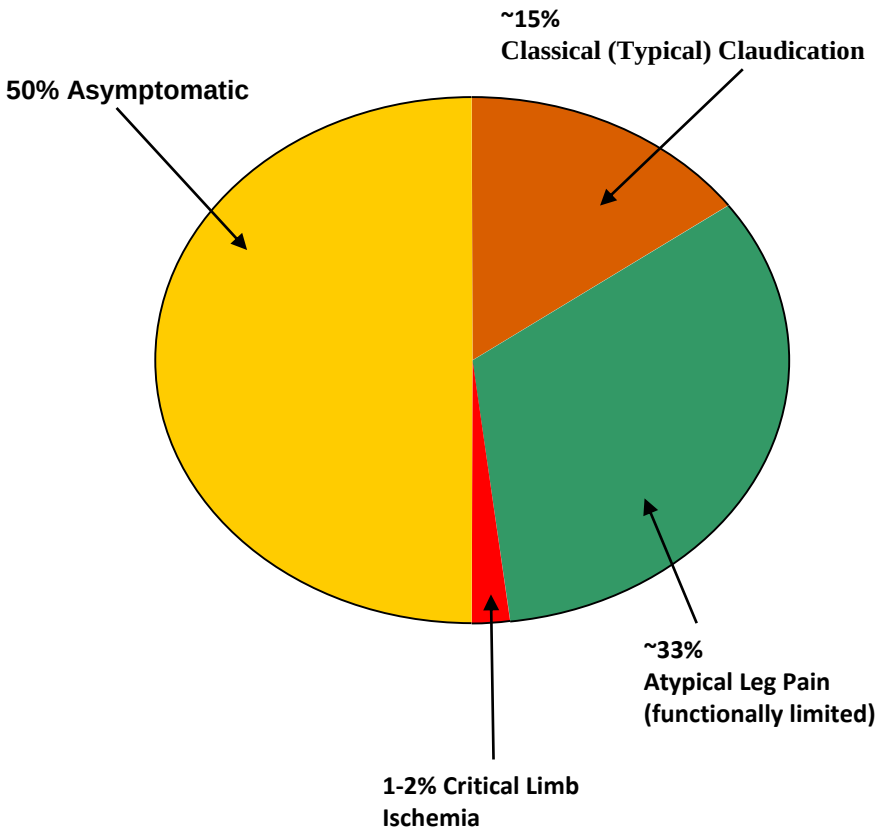
Clinical Presentation in Women





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Natural History of Lower Extremity Outcomes in Women

- **Women have lower extremity functional impairment which leads to Poor functional performance**
  - Lower gender based length strength
  - Poorer cardiopulmonary fitness
  - Reduced calf muscle hemoglobin, O2 saturation
  - Have other co morbidities:
    - Depression
    - Hypothyroidism
    - Arthritis/Osteoporosis

Ethnic and Social Distribution of Clinical Presentation

- Minority women far worse than white women
  - The interaction of biology and environment
    - Smoking/Diet/Physical Inactivity/ Hypertension/ Less Access to Care
    - Higher prevalence of diabetes
    - More advanced disease of PAD
    - Worse outcome with Therapy
      - Higher graft failure in African-American Women
      - Hispanic ethnicity is an independent predictor of limb loss in women undergoing autogenous infrainguinal Bypass

Treatment Options for PAD

The goals of PAD treatment are to manage symptoms and to stop the progression of atherosclerosis to reduce risk of heart attack and stroke.

1 Lifestyle Changes

- Healthy diet
- Smoking cessation
- Exercise/walking program
- Diabetes therapy

2 Medications

- Cardiovascular Risk Reduction
- Helping increase walking distance

3 Revascularization

- Percutaneous endovascular treatment
- Bypass surgery

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Source: Hirsch AT, et al. Circulation. 2006;113:e463-e665.

Medical Treatment

- Cilostazol the only FDA approved drug
  - Not well tested in women
  - Moderate efficacy for men and women
- Exercise therapy : Supervised Exercise Therapy (SET) versus Home Based Exercise Therapy (HBET)

EXERCISE THERAPY AND PAD

- Cochrane Database syt rev 2018:(Hageman et al)
  - 21 trials: 1400 participants : 35% women
    - SET better than HBET (MWD doubled)
    - Adherence was 80%
    - No effect on mortality
    - No good data on QOL or Functional impairment
- Dua et al (J Vasc surg 2019) : Lack of availability
    - Offered thru Cardiac Rehab
    - Travel distance
    - Low reimbursement rates

Gender and Patient Selection for Lower Extremity Revascularlization

- Men are twice as likely selected for revascularization (including hospital inpatients presenting with PAD)
- Women selected are
  - Older and have more advanced disease
  - Lower prevalence of smoking
  - Higher proportion of suprainguinal procedures
  - Lower rates of bypass to tibial arteries
  - Similar TASC Classification [C/D]
  - Treated mostly for rest pain (16% vs 11%)

Influence of Gender on Outcomes Associated with Vessel Patency

- Inferior Patency
  - Aortoiliac disease: RR: 4.6 for bypass and stent thrombosis in women (Ballard and Co.)
  - 5 year cumulative patency rate for above the knee fem-pop bypass
    - 61% vs. 37% for men (large vs. small graft)
    - 45% in women (both sizes) (Green & al.)
  - African-American Women had the lowest patency rate after (SVG Bypass) at 1 year. (Ngyuen et al.)

Survival/Amputation Free Survival /QOL

- Data is inconsistent
  - Gender is often cofounder for:
    - Morbidity
    - Age
    - Procedural factors
  - Multiple studies have reported similar amputation free survival rate (Mean 61.5 month)
  - QOL is similar

Perioperative Adverse Events

- Higher rates of perioperative wound complications in women (13.5% vs. 3.3%) (Belkin et al.)
- Increased length of hospital stay
- Lower quality of Life
- Significant higher incidence of perioperative MI in women undergoing infrainguinal bypass. (9.8% vs 2%) (Mays et al.)

Endovascular Treatment

- Yin J et al. [Society for Vascular Surgery 2017 San Diego] [12338 patients 41% Women for fem-pop]
  - Present later in the disease process
  - Had lower ABI index
  - Technical success is the same
  - No difference in mortality, stroke or MI rate
  - Higher rate of vascular complications (Bleeding)
  - High rate of 1 year re-intervention (primary patency at 1 year: 73% vs 79%)
  - At 1 year women less likely to be ambulatory

Drug Coated Balloon Trials

- THUNDER Trial
  - Men = Women
  - Short term improvement in outcomes after DCB
  - At 5 year TLR rate was similar in women in DCB versus standard PTA
- LEVANT 2 Trial
  - Women did better with standard PTA
- IN.PACT SFA Trial
  - no difference between the groups

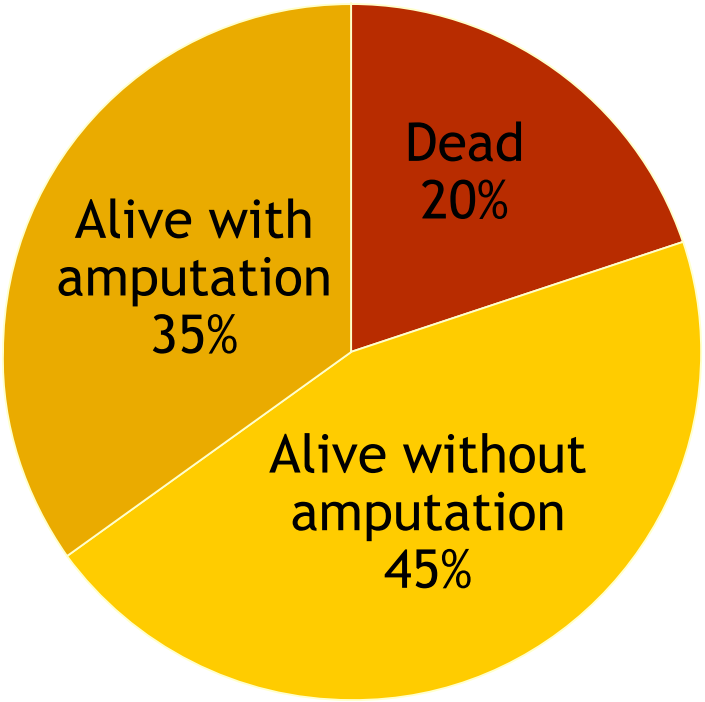
CONFIRM Registries

- 3131 Patients
  - 1261 Women: mean age 73 years
  - Patients treated with orbital atherectomy
    - Women were older
    - Higher rate of CLI
    - Success rate was similar
    - Higher rate of all types of dissection (mostly flow limiting)

Critical Limb Ischemia

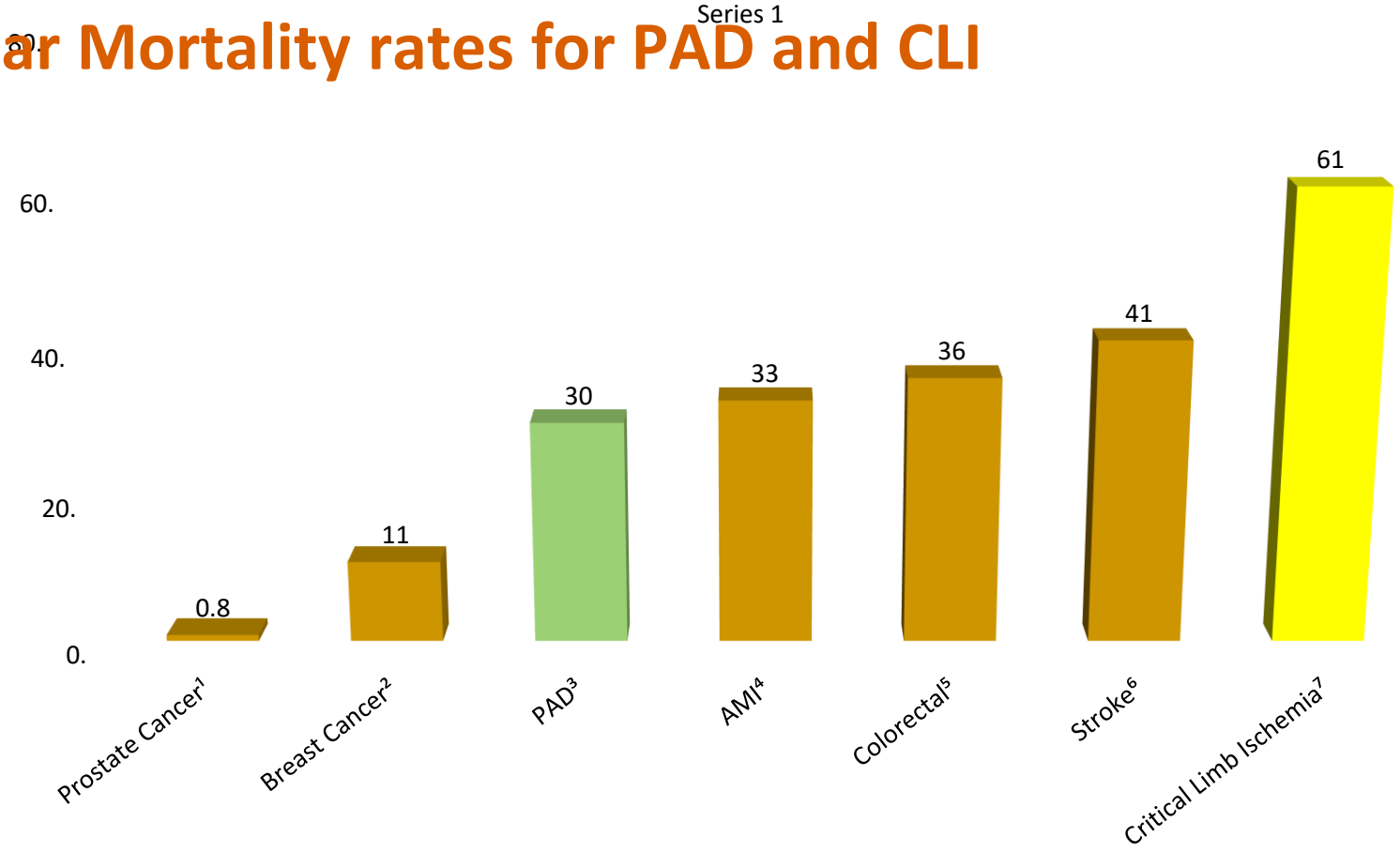
Fate of Patients With CLI After Initial Treatment

Summary of 6-month outcomes from 19 studies



Critical limb ischemia is defined as ischemic rest pain, non-healing wounds, or gangrene.

5 Year Mortality rates for PAD and CLI



1. SEER Stat Fact Sheets: Prostate. National Cancer Institute Web site. http://seer.cancer.gov/statfacts/html/prost.html. Accessed April 24, 2013.
2. SEER Stat Fact Sheets: Breast. National Cancer Center Institute Web site. http://seer.cancer.gov/statfacts/html/breast.html. Accessed April 24, 2013.
3. Herlitz J, Hjalmarson A, Karlson BW, et al. 5-year mortality rate in patients with suspected acute myocardial infarction in relation to early diagnosis. *Cardiology*. 1988;75(4):250-9.
4. Weitz JI, Byrne, J, Clagett GP, et al. Diagnosis and Treatment of Chronic Arterial Insufficiency of the Lower Extremities: A Critical Review *Circulation*.1996;94:3026-3049.
5. SEER Stat Fact Sheets: Colon and Rectum. National Cancer Institute Web site. http://seer.cancer.gov/statfacts/html/colorect.html. Accessed April 24, 2013.
6. Hartmann A, Rundek T, Mast H, et al. Mortality and causes of death after first ischemic stroke: the Northern Manhattan Stroke Study. *Neurology*. 2001;57:2000-2005.
7. Ljungman C, et al.*Eur J Vasc Endovasc Surg*. 1996;11:176-182.

Early Detection of PAD is Key to Patient Survival

Detection through available tools such as Ankle Brachial Index (ABI), and angiography is key to detect PAD early.

65% of patients undergoing limb amputation in the U.S. did not have an ABI documented

Mortality Rates post-amputation from vascular disease			
30 day	1 year	3 years	5 years
9 -15%	60%	42%	35-45%

Sources: www.amputee-coalition.org/healthcare-providers/limb-loss-statistics/index.html, Hirsch AT, :Circulation. 2007;116:2086-2094 Endovascular Today, March 2006

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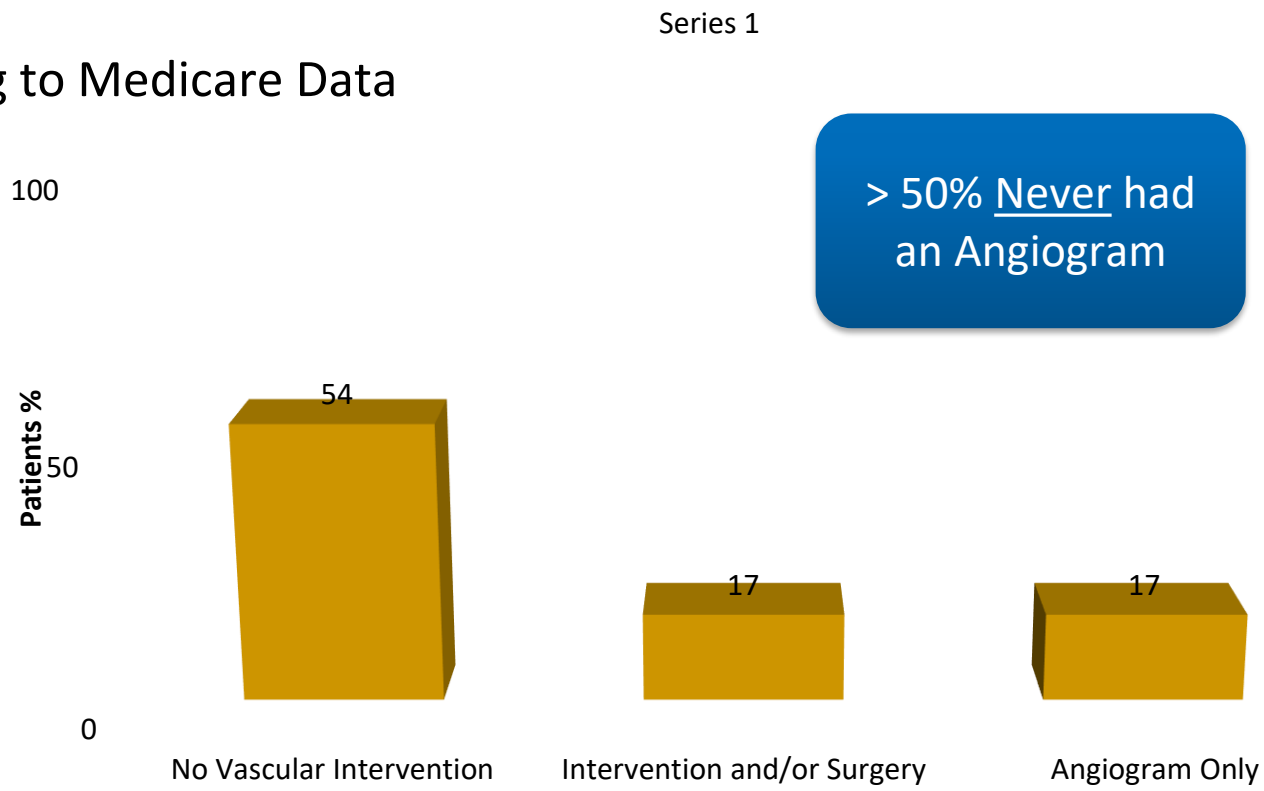
Angiograms and Revascularization are Underutilized Prior to Amputation[1]

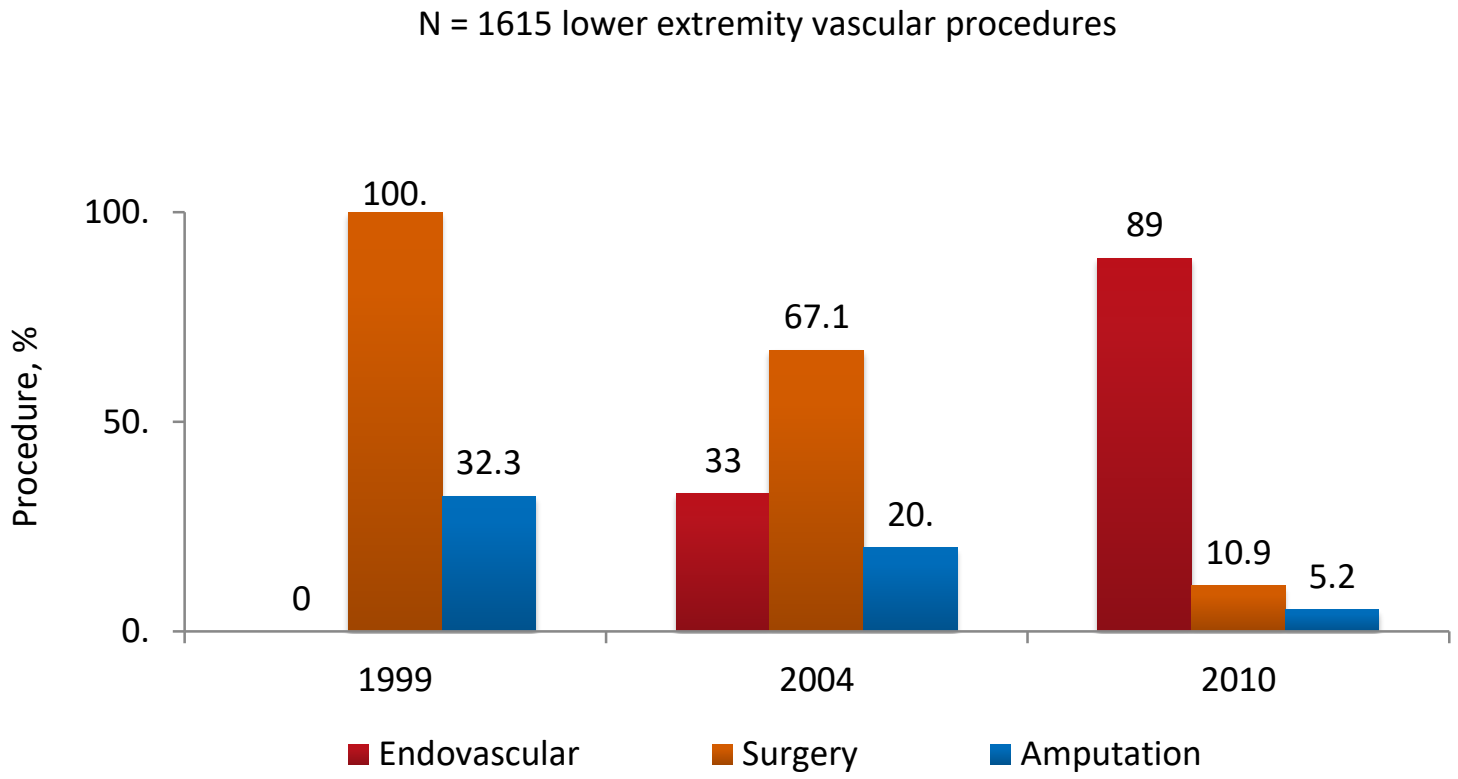
According to Medicare Data



N = 20,464 Patients with PAD who underwent major leg amputation (2003 – 2006)

1. Goodney PP, Travis LL, Nallamothu BK, et al. *Circ*: Cardiovasc Qual Outcomes

Amputation rates decrease as Revascularization rates increase



1. Balar NN, Dodla R, Oza P, et al. Endovascular Versus Open Revascularization for Peripheral Arterial Disease. *Endovascular Today.* 2011:61-64

Women and CLI

- Women present at an older age
- More advanced disease: multilevel
- Female gender is an independent prediction for severe and diffuse disease:
  - Atypical symptoms
  - More rapid progression of the disease in post menopasual women
  - Social factors: Living alone and Nursing homes.

Women and CLI

- Less likely to undergo revascularization
- Higher ratio of above the knee amputation
- Higher 30 day mortality and major amputation following revascularization (endo/surgery)
- Higher perioperative mortality

Summary

- 8-12 million Americans have PAD
- Common risk factors;
  - Smoking
  - Diabetes
  - Hypertension
  - Hyperlipidemia
  - Increased age
- CAD and CVD are common in patients with PVD
- If untreated PAD can lead to:
  - Decrease in quality of life
  - Increase in amputation rate
  - Increase in related CV events

Summary

- Exact prevalence of PAD in women is unknown but seems to be equal as in men (4.2% vs. 4.5%)
- Burden of the disease is larger
- Morbidity and mortality events rates trend higher
- Women are under represented in trials (20% average).
- Possible association between female gender and adverse outcomes with PAD revascularization.

Summary

- Awareness of PAD in women and men is strikingly low compared to other CVD and general disease
- Current data suggest that women may be somewhat more aware
- An improvement or elimination of this knowledge gap is needed
  - PAD is addressed in government sponsored education but not as distant topic.
  - Increase cross communication between women heart health programs and PAD awareness
  - Emphasis that PAD is a distinct disease not really a risk factor for CVD.

Recommendations

- Primary care providers including gynecologists should identify women with high risk for PAD by targeted review of vascular symptoms, physical examination and diagnostic testing (ABI)
- Women at risk for PAD should be informed of PAD risk factors, symptoms and CV risk
- Women CV health programs should include PAD awareness campaigns
- Increase the potential role of women in facilitating improved PAD awareness
- Translate the success for “Go Red for Women” campaign and use it as a way to achieve comparable success

Guidance for PAD diagnosis

- Step 1
  - Assess patient for risk factors
    - Smoking
    - Diabetes
    - Hypertension
    - Age: Men >55 years and women >65 years
    - Hyperlipidemia
    - History of cardiovascular disease
  - Assess patient for leg symptoms
    - Intermittent claudication
    - Critical limb ischemia
  - Tools: PAD checklist, Rose questionnaire, Edinburgh questionnaire
- Step 2
  - If suspicion of PAD, perform an ABI to confirm diagnosis using a hand-held Doppler

Recommendations

- Future studies of PAD prevalence are needed.
- Future PAD diagnostic tool investigation should include adequate gender based samples to assess the sensitivity, specificity, and accuracy of each test
- Future research on the potential of gender on the biology of atherosclerosis, aneurysmal disease and thrombosis
- Clinical trials should recruit and enroll female participates at a rate that reflects the population prevalence of women in the symptomatic population

Thank You

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