

Critical Limb Ischemia: Key Differences Compared to the Claudicant

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Disclosures:

BMS-Sanofi: Speaker's Bureau, Consulting

Merck: Speaker's Bureau

GSK: Speaker's Bureau

Critical Limb Ischemia = Vascular Urgency

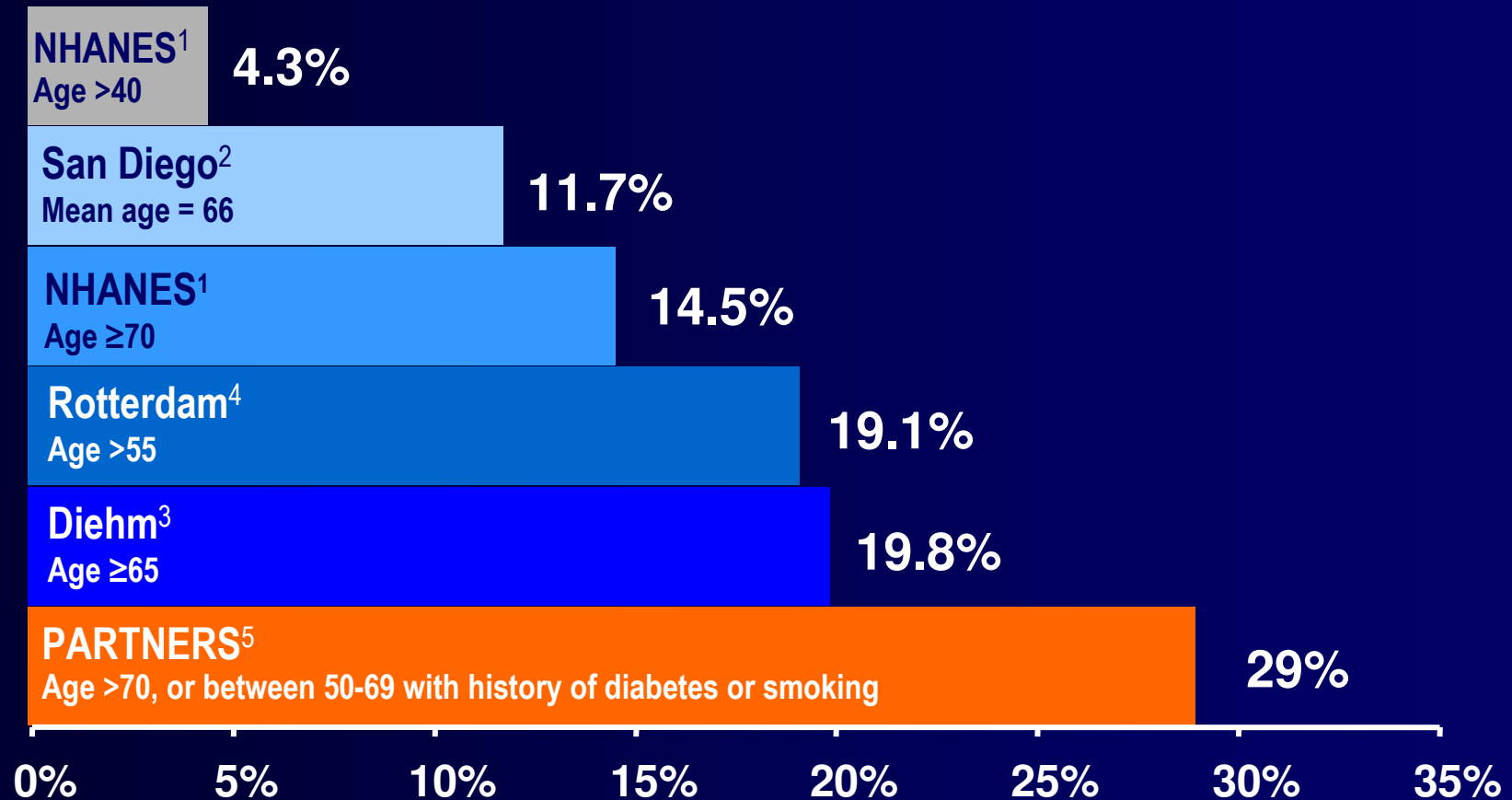
- Ischemic Rest pain
- Non-healing ulcer
- Gangrene



Agenda

- **Prevalence of CLI**
- **CLI Demography**
- **Medical Therapy**

Peripheral Arterial Disease: *Prevalence*



NHANES = National Health and Nutrition Examination Survey. PARTNERS = PAD Awareness, Risk, and Treatment New Resources for Survival program.

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

Manifestations of PAD in Sweden

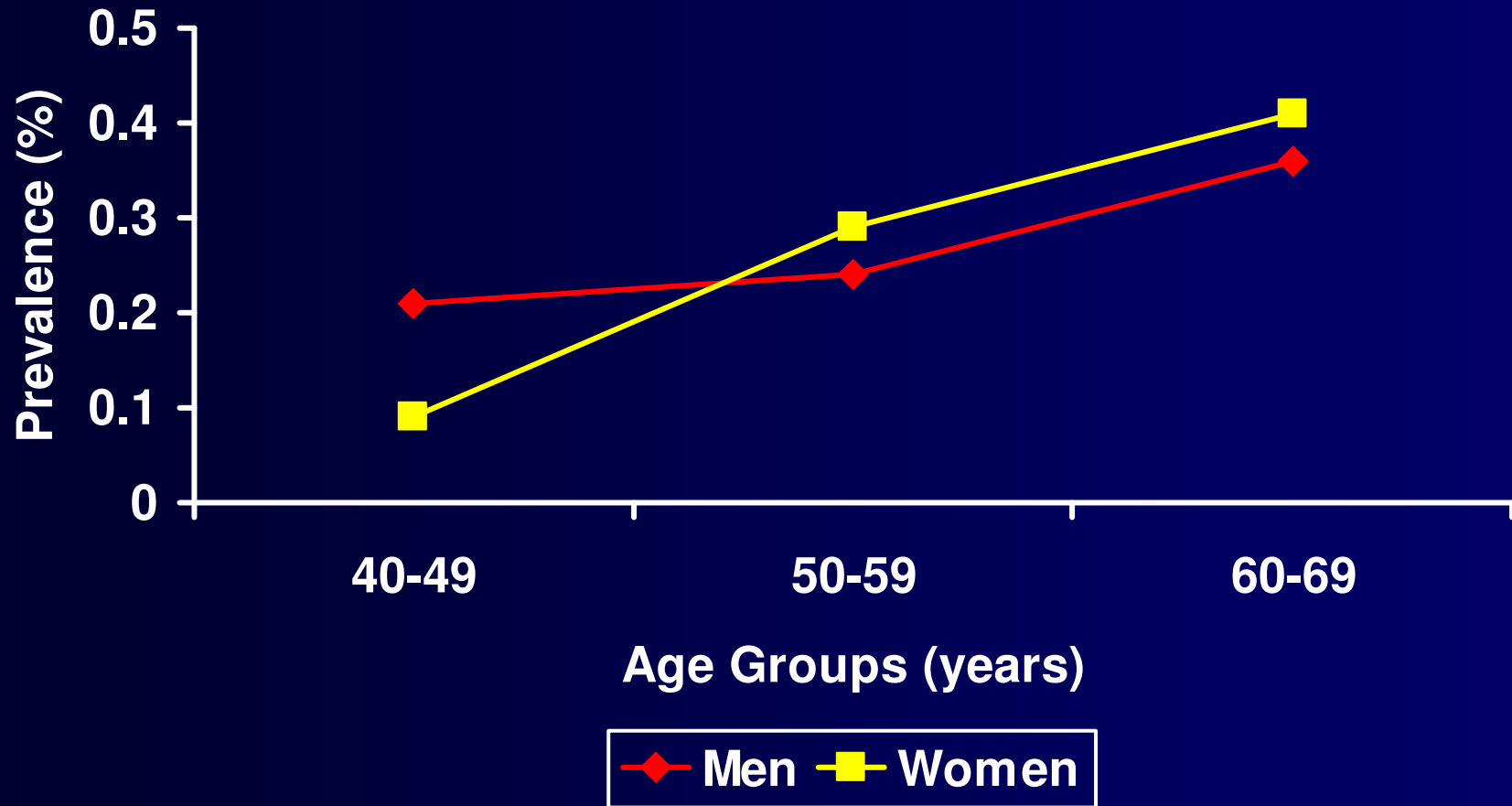
8000 Swedish women and men, aged 60 to 90 years were analyzed for presence of PAD according to reported symptoms and an ABI <0.9.

Table IV. Peripheral arterial disease prevalence by gender and stage of disease

<i>Stage of PAD</i>	<i>Total</i>
Peripheral arterial disease (all with ABI <0.9)	18.0 (16.0-19.9)
Asymptomatic PAD (all with ABI <0.9 without symptoms)	11.1 (9.5-12.8)
Intermittent claudication (all with ABI <0.9 and positive Rose Q)	6.8 (6.5-7.1)
Severe ischemia 1 (all with ankle BP <70 mm Hg)	1.2 (1.0-1.4)
Severe ischemia 2 [‡] (all with ankle BP <70 mm Hg and rest pain)	0.4

Incidence of CLI in Norway

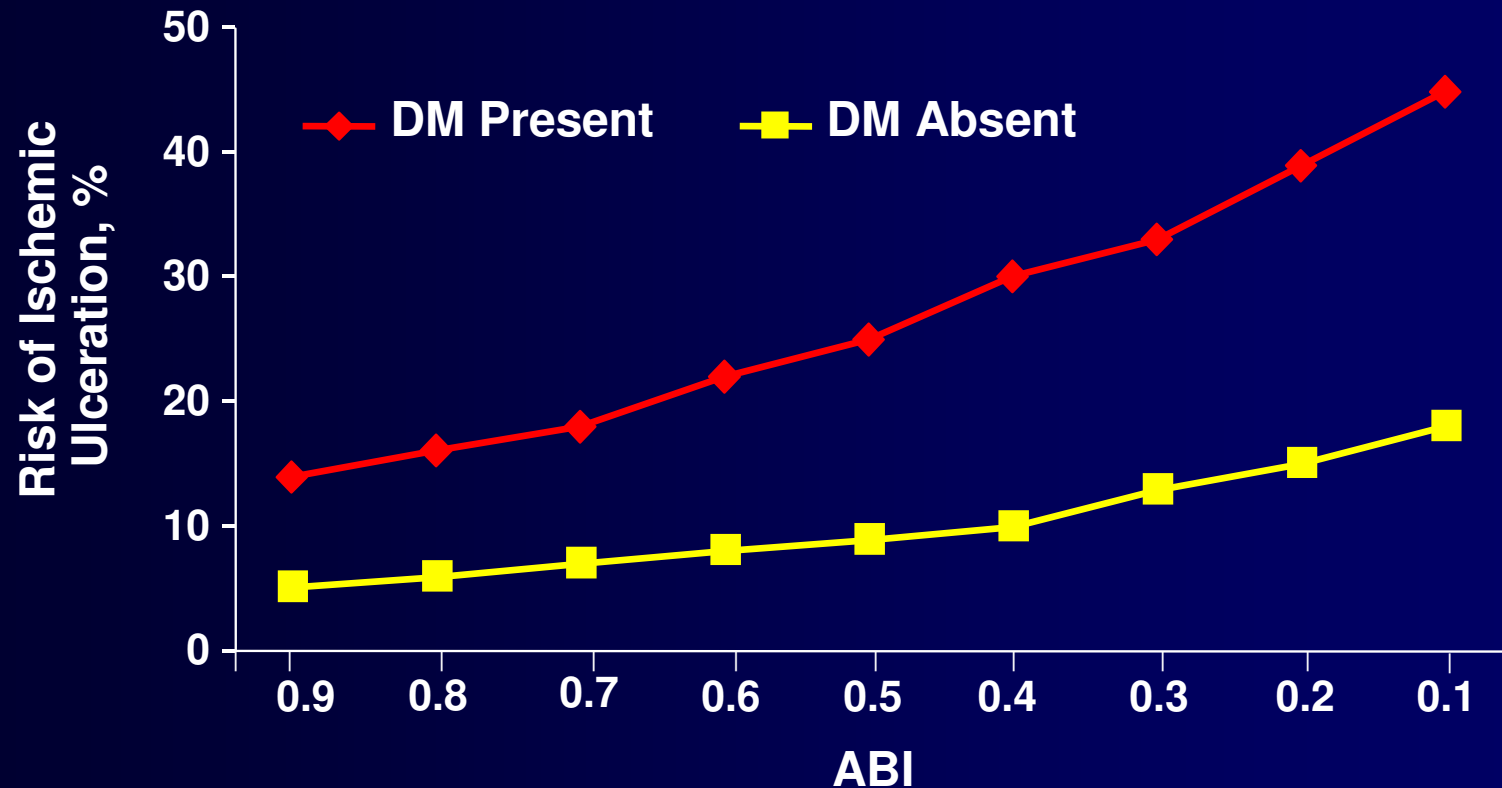
Unselected screening of 20, 291 participants in 4 cities in Norway.
CLI diagnosed with ulcers or supine rest pain in foot.



Jensen, SA. Eur J Vasc Endovasc Surg 2006;32:60

5-Year Risk of Developing Ischemic Ulceration

N=1244 men with claudication

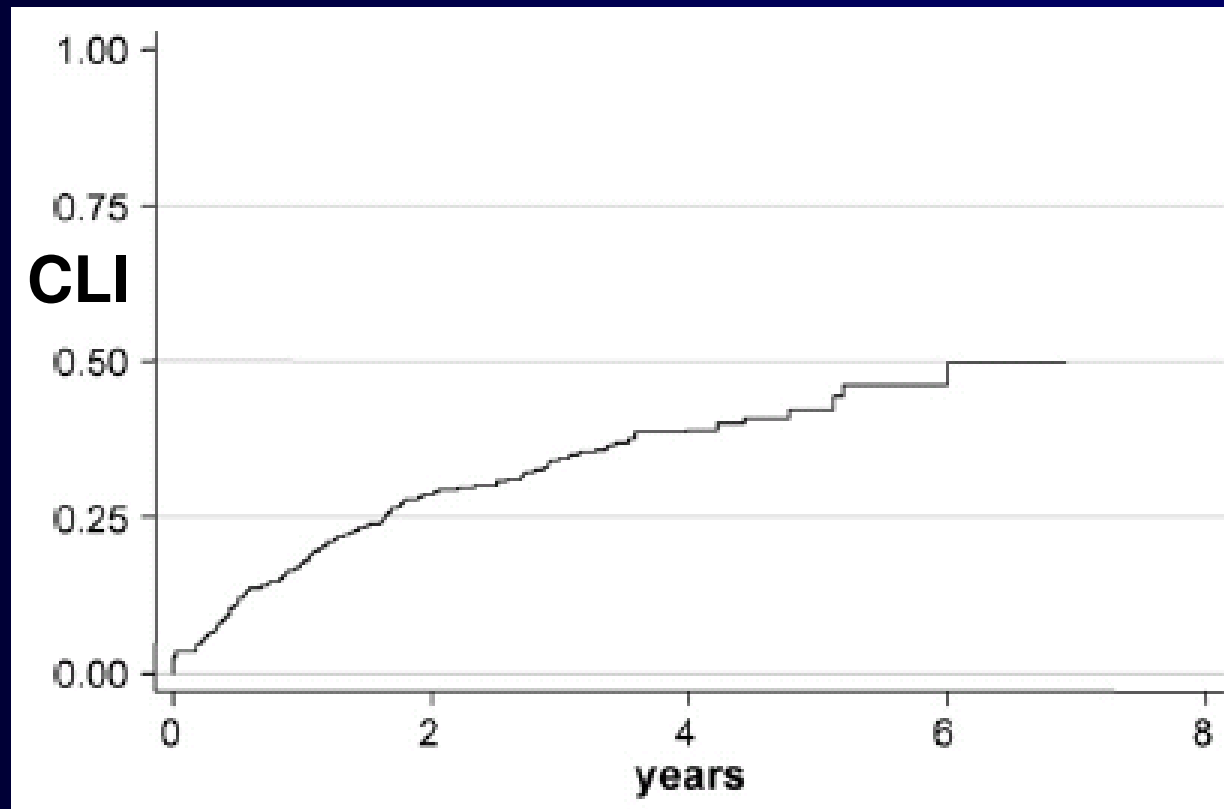


DM = Diabetes mellitus

Modified with permission from Aquino R. *J Vasc Surg.* 2001;34:962-970.

Incidence of Contralateral CLI in Diabetic Subjects

incidence of CLI and amputation of the contralateral limb in 533 diabetic pts hospitalized because of CLI from 1999 to 2003 and followed-up until 2005.



PREVENT III: A Snapshot of Limb Salvage Bypass Surgery

- Randomized, placebo-controlled trial of E2F-decoy ODN for the prevention of vein graft failure
- Patients undergoing autogenous vein bypass surgery for treatment of CLI
 - Broadly inclusive study population
- 83 North American sites (academic and community hospitals) including 5 sites in Canada
- Enrollment initiated December 2001
- Completed enrollment September 2003 (N=1404)
- One year follow-up

Conte MS, et al. *Vasc Endovasc Surg* 2005
Conte MS, et al. *J Vasc Surg* 2006

PREVENT III
 STUDY OF E2F DECOY IN THE PREVENTION OF VEIN GRAFT FAILURE

PREVENT III: Demographics

	Edifoligide (n=707)	Placebo (n=697)
Age (yr) Mean \pm SD	68.7+/-11.68	68.3+/-11.42
Male	454 (64.2%)	443 (63.6%)
Caucasian	526 (74.4%)	491 (70.4%)
Black	116 (16.4%)	133 (19.1%)
Asian	3 (0.4%)	7 (1.0%)
Hispanic	53 (7.5%)	54 (7.7%)
Other	9 (1.3%)	12 (1.7%)
CLI criterion- Rest Pain	184 (26.0%)	169 (24.2%)
Non-healing Ulcer	272 (38.6%)	280 (40.2%)
Gangrene	247 (34.9%)	246 (35.3%)
ABI- Mean/Median	0.5/0.4	0.5/0.4

PREVENT III: Comorbidities

Comorbidities

Hypertension 577 (81.6%) 569 (81.6%)

Diabetes 461 (65.2%) 439 (63.0%)

CAD 338 (47.8%) 336 (48.2%)

CVD 144 (20.4%) 140 (20.1%)

Smoking 520 (73.5%) 513 (73.6%)

Dyslipidemia 393 (55.6%) 373 (53.5%)

Dialysis 84 (11.9%) 86 (12.3%)

Prior leg revascularization

Inflow procedure 146 (20.7%) 147 (21.1%)

Infrainguinal (either limb) 190 (26.9%) 193 (27.7%)

Perioperative (30 day) complications

	Edifoligide	Placebo	Total
Total major morbidity	124 (17.3%)	126 (17.9%)	250 (17.6%)
Cardiac or resp arrest	12 (1.7%)	9 (1.3%)	21 (1.5%)
DVT	6 (<1.0%)	8 (1.1%)	14 (<1.0%)
Death	20 (2.8%)	18 (2.6%)	38 (2.7%)
Graft occlusion	30 (4.2%)	43 (6.2%)	73 (5.2%)
Major amputation	13 (1.8%)	12 (1.7%)	25 (1.8%)
Pneumonia	10 (1.4%)	14 (2.0%)	24 (1.7%)
Pulmonary embolism	1 (<1.0%)	0 (0.0%)	1 (<1.0%)
Stroke or TIA	12 (1.7%)	8 (1.1%)	20 (1.4%)
Major wound complication	38 (5.3%)	30 (4.3%)	68 (4.8%)
Dehiscence	3 (<1.0%)	9 (1.3%)	12 (<1.0%)
Infection	25 (3.5%)	15 (2.1%)	40 (2.8%)
Necrosis	9 (1.3%)	6 (<1.0%)	15 (1.1%)
Graft hemorrhage	3 (0.4%)	4 (0.6%)	7 (0.5%)

CLI: Treatment Goals

- **Minimize risk of other major CV events**
- **Relief of pain**
- **Healing of wounds**
- **Preservation of a functional limb**

CLI: Treatment Modalities

- **Medical therapy: limited role**
 - Prostanoids, novel pharmaceuticals
 - Therapeutic angiogenesis
- **Limb Revascularization**
 - Endovascular options
 - Surgical options
 - Combination approaches
- **Wound healing adjuncts**

Summary

- **Critical (or Chronic) limb ischemia is uncommon, even in PAD patients**
- **Pay close attention to diabetic patients**
- **Medical therapies have a role in chronic cardiovascular risk reduction**
- **Medical therapy has a limited role in CLI resolution**