

References:

Berger JS, Krantz MJ, Kittelson JM, Hiatt WR. Aspirin for the prevention of cardiovascular events in patients with peripheral artery disease. A meta-analysis of randomized trials. *JAMA* 2009;301:1909–1919.

Breek JC, Hamming JF, De Vries J, Aquarius AD, van Berge Henegouwen DP. Quality of life in patients with intermittent claudication using the World Health Organization (WHO) questionnaire. *eur J Vasc endovasc Surg* 2001;21:118–122

CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet* 1996;348:1329–39.

Cilostazol. Micromedex DrugDex. Accessed 10/14/2011.

http://www.thomsonhc.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/192D1F/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/0B00E5/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DoIntegratedSearch?SearchTerm=cilostazol

Criqui MH, Langer RD, Fronek A, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med* 1992;326:381–6.

Dawson DL, Cutler BS, Hiatt WR, et al. A comparison of cilostazol and pentoxifylline for treating intermittent claudication. *Am J Med* 2000;109:523–530.

Gardner AW, Poehlman ET. Exercise rehabilitation programs for the treatment of claudication pain: a meta-analysis. *JAMA* 1995;274:975-980

Goldhaber SZ, Manson JE, Stampfer MF, et al. low-dose aspirin and subsequent peripheral arterial surgery in the Physician's Health Study. *Lancet* 1992;340:143–145.

Heart Protection Study Collaborative Group. Randomized trial of the effects of cholesterol lowering with simvastatin on peripheral vascular and other major vascular outcomes in 20,536 people with peripheral arterial disease and other high-risk conditions. *J Vasc Surg* 2007;45:645–54.

Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 2001;286:1317-24.

Hirsch AT, Haskal ZJ, Hertzner NR, Bakal CW, Creager MA, Halperin JL, Hiratzka LF, Murphy WR, Olin JW, Puschett JB, Rosenfield KA, Sacks D, Stanley JC, Taylor LM Jr, White CJ, White J, White RA, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Hunt SA, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B; American Association for Vascular Surgery; Society for Vascular Surgery; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society of Interventional Radiology; ACC/AHA Task Force on Practice Guidelines Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease; American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; Vascular Disease Foundation. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation*. 2006 Mar 21;113(11):e463-654.

Jonason R, Bergstrom R. Cessation of smoking in patients with intermittent claudication. *Acta Med Scand* 1987;221:253–60.

Lane DA and Lip GYH. Treatment of hypertension in peripheral arterial disease. *Cochrane Database of Systematic Reviews* 2009 Oct 7;(4):CD003075.

Meijer WT, Hoes AW, Rutgers D, Bots ML, Hofman A, Grobbee DE. Peripheral arterial disease in the elderly: the Rotterdam Study. *Arterioscler thromb Vasc Biol* 1998;18:185–92.

Ostergren J, Sleight P, Dagenais G, Danisa K, Bosch J, Qilong Y, Yusuf S, HOPE study investigators. Impact of ramipril in patients with evidence of clinical or subclinical peripheral arterial disease. *European Heart Journal* 2004;25(1):17–24.

Pentoxifylline. Micromedex DrugDex. Accessed 10/14/2011.

<http://www.thomsonhc.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch>

Radack K, Deck C. Beta-adrenergic blocker therapy does not worsen intermittent claudication in subjects with peripheral arterial disease: a meta-analysis of randomized controlled trials. *Arch Intern Med* 1991;151:1769-76.

Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. *New England Journal of Medicine* 2000;342(3):145–53.

PAD Severity as a Predictor of Cardiovascular Outcomes

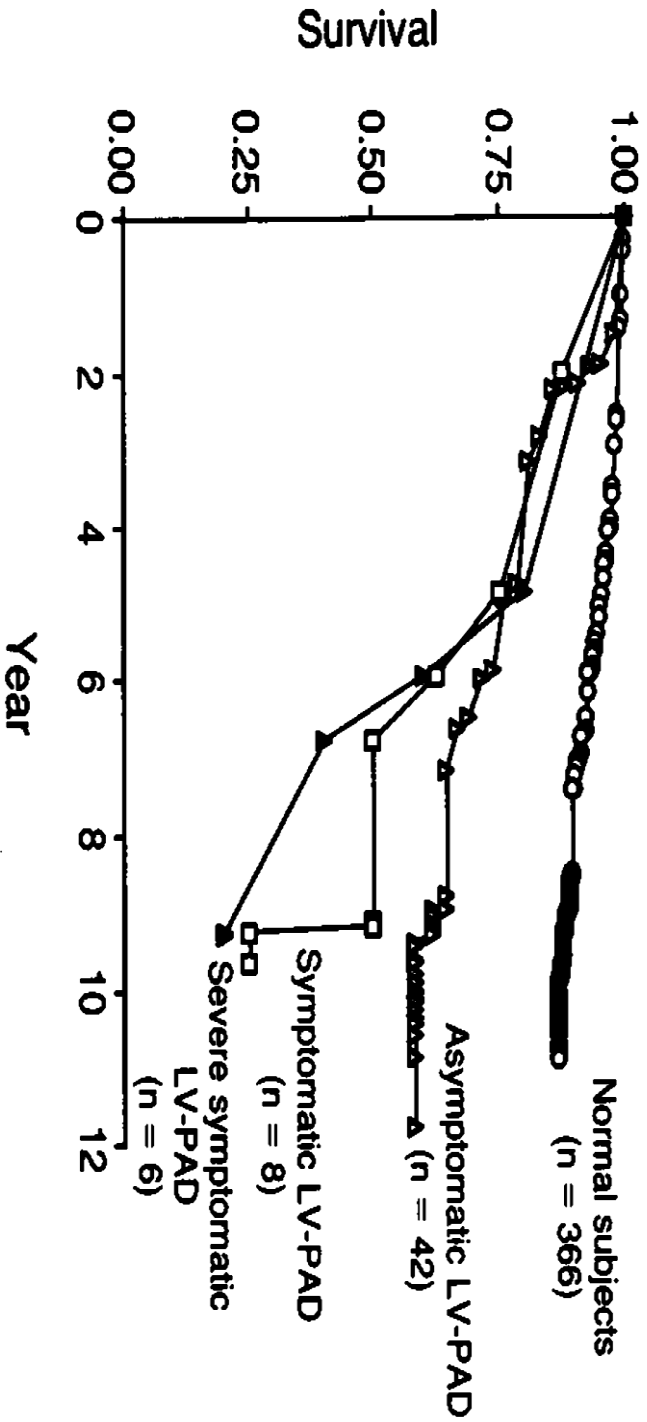


Figure 2. Kaplan—Meier Survival Curves Based on Mortality from All Causes among Normal Subjects and Subjects with Symptomatic or Asymptomatic Large-Vessel Peripheral Arterial Disease (LV-PAD), after the Exclusion of Subjects with Evidence of Cardiovascular Disease at Base Line.

HOPE Study Results Yusuf, 2000

| Outcome | Asymptomatic PAD | | | | Symptomatic PAD | |
|---------------------------|----------------------------------|---------|----------------------------------|---------|-----------------|---------|
| | ABI 0.6 – 0.9 (Mild) n = 1391 | | ABI <0.6 (Mod-Severe) n = 727 | | n = 1725 | |
| Study Arm | Ramipril | Placebo | Ramipril | Placebo | Ramipril | Placebo |
| Primary Outcome (%) | 15.7 | 21.6 | 16.4 | 22.0 | 20.1 | 25.8 |
| Myocardial Infarction (%) | 12.3 | 15.2 | 11.2 | 15.5 | 12.3 | 16.1 |
| Stroke (%) | 2.6 | 6.0 | 5.4 | 6.4 | 6.2 | 8.3 |
| CV Death (%) | 6.3 | 10.8 | 8.2 | 10.4 | 10.4 | 13.6 |
| All-cause Death (%) | 9.6 | 15.9 | 13.2 | 16.2 | 16.7 | 19.74 |

Outcome rates for ramipril and placebo in the HOPE trial stratified by PAD severity. Statistical significance is denoted by the red boxes.

Kaplan-Meier Rates

