

Aspirin Evidence: Primary Prevention in Men

Physicians' Health Study (PHS)

22,071 men randomized to aspirin (325mg every other day) followed for an average of 5 years

End point	Relative Risk (95% CI)	P value
Myocardial infarction		
Fatal	0.34 (0.15 -0.75)	0.007
Nonfatal	0.59 (0.47 -0.74)	<0.00001
Total	0.56 (0.45 -0.70)	<0.00001
Stroke		
Fatal	1.51 (0.54 -4.28)	0.43
Nonfatal	1.20 (0.91 -1.59)	0.20
Total	1.22 (0.93 -1.60)	0.15

Aspirin significantly reduces the risk of MI in men

CI=Confidence interval, MI=Myocardial infarction

Physicians' Health Study Research Group. *NEJM*
1989;321:129-35

Aspirin Evidence: Primary Prevention in Women

Womens' Health Study (WHS)

39,876 women randomized to aspirin (100 mg every other day) or placebo for an average of 10 years



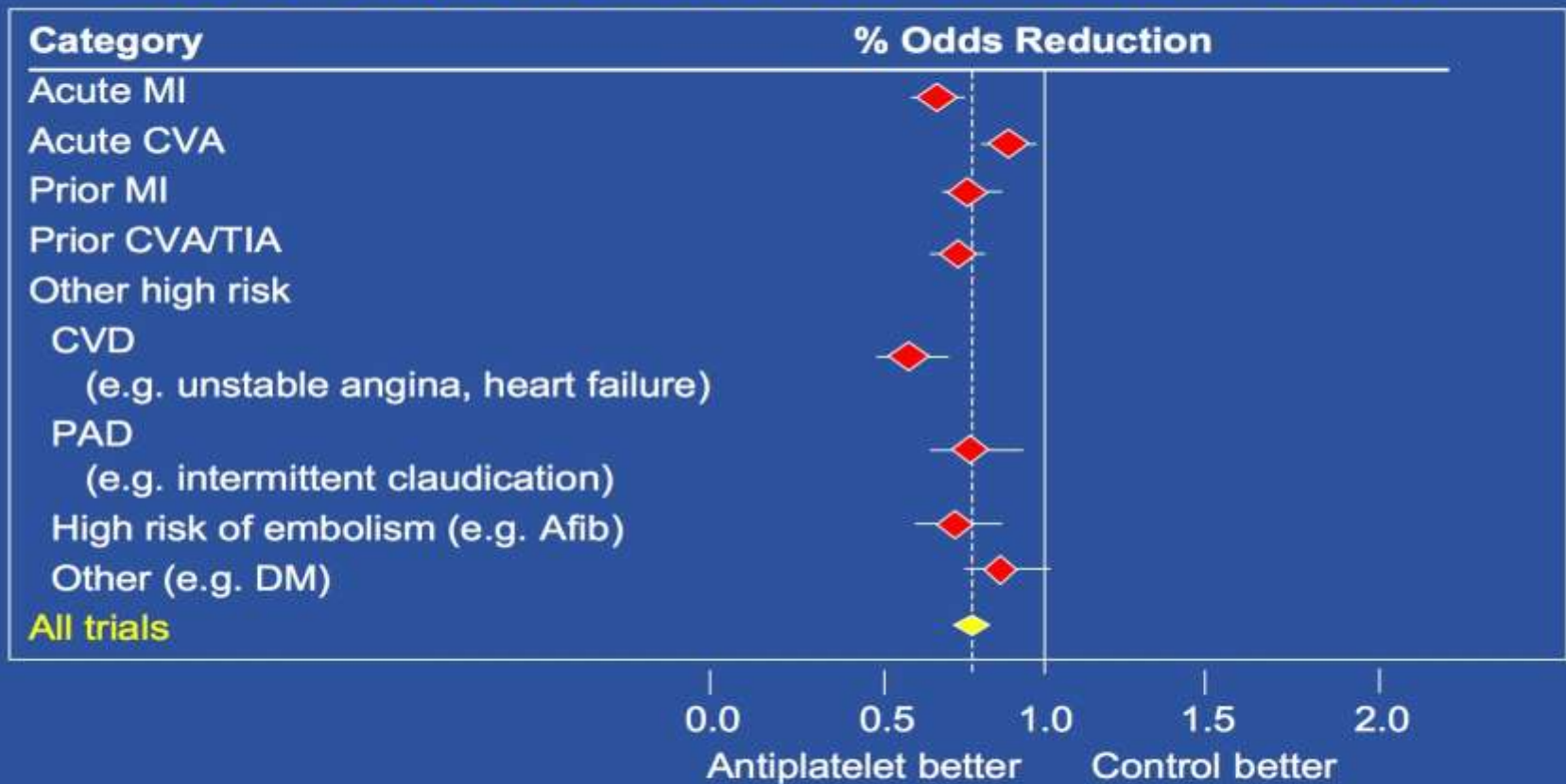
Aspirin does not reduce the risk of MI in low risk women

MI=Myocardial infarction

Ridker P et al. *NEJM* 2005;352:1293-304

Aspirin Evidence: Secondary Prevention

Effect of antiplatelet treatment* on vascular events**



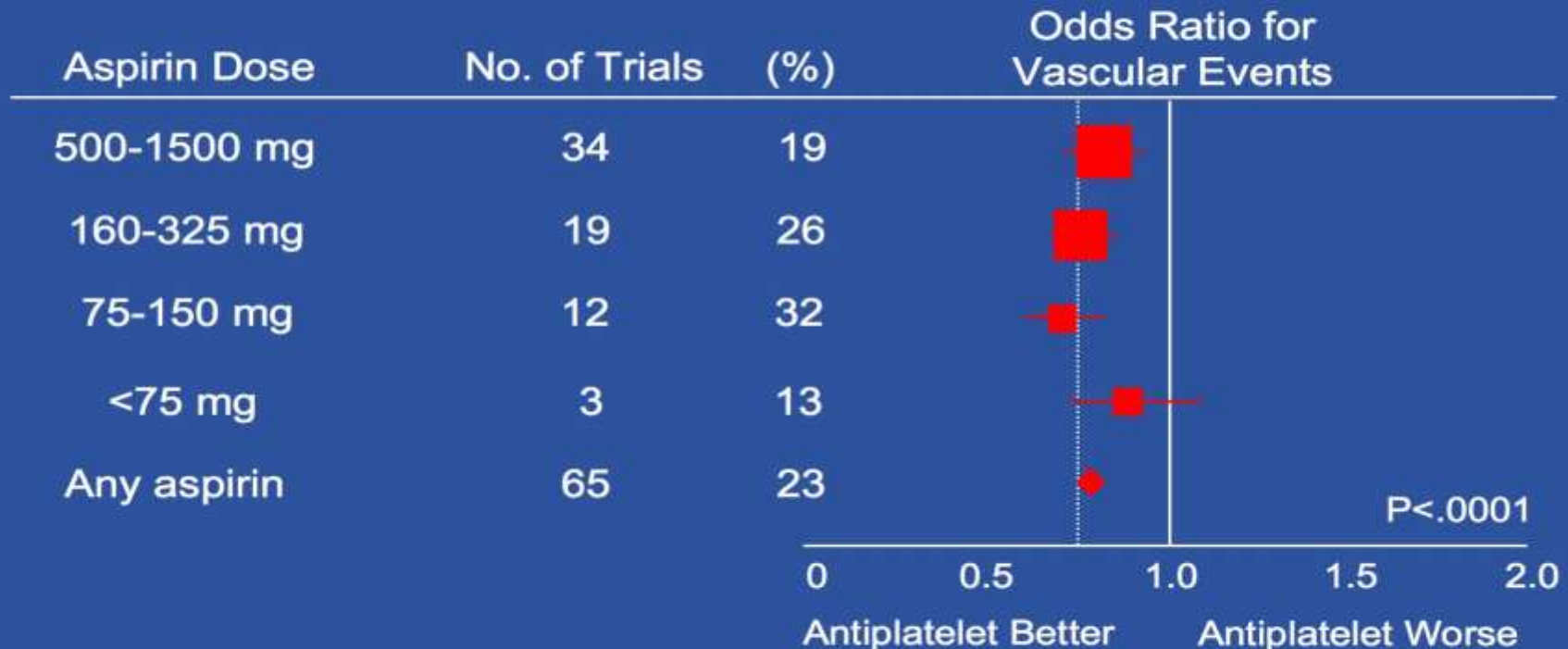
*Aspirin was the predominant antiplatelet agent studied

**Include MI, stroke, or death

Antithrombotic Trialist Collaboration. *BMJ* 2002;324:71–86

Aspirin Evidence: Dose and Efficacy

Indirect comparisons of aspirin doses on vascular events in high-risk patients



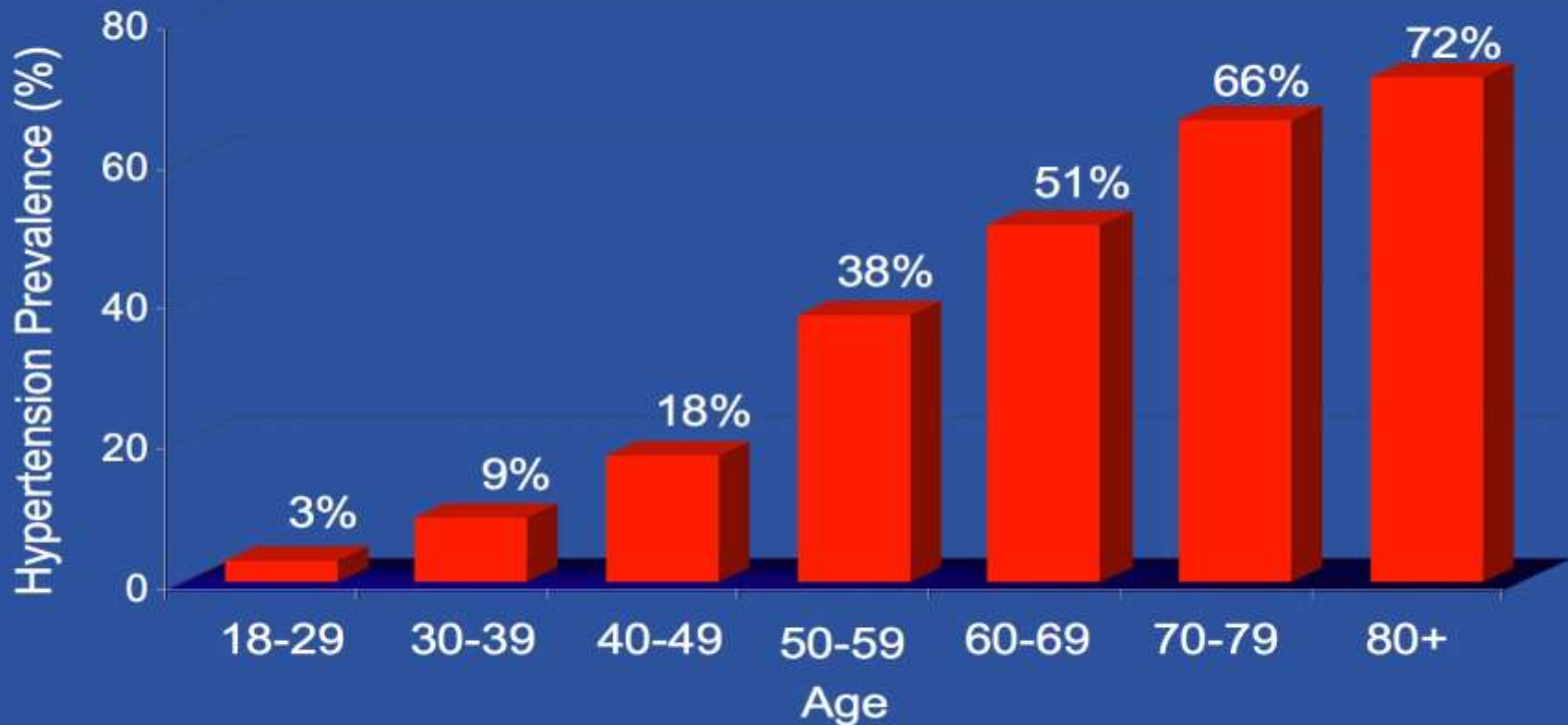
Antithrombotic Trialist Collaboration. *BMJ* 2002;324:71-86

Blood Pressure Evidence



Blood Pressure: Risk Increases with Age

National Health and Nutrition Examination Survey (NHANES) III

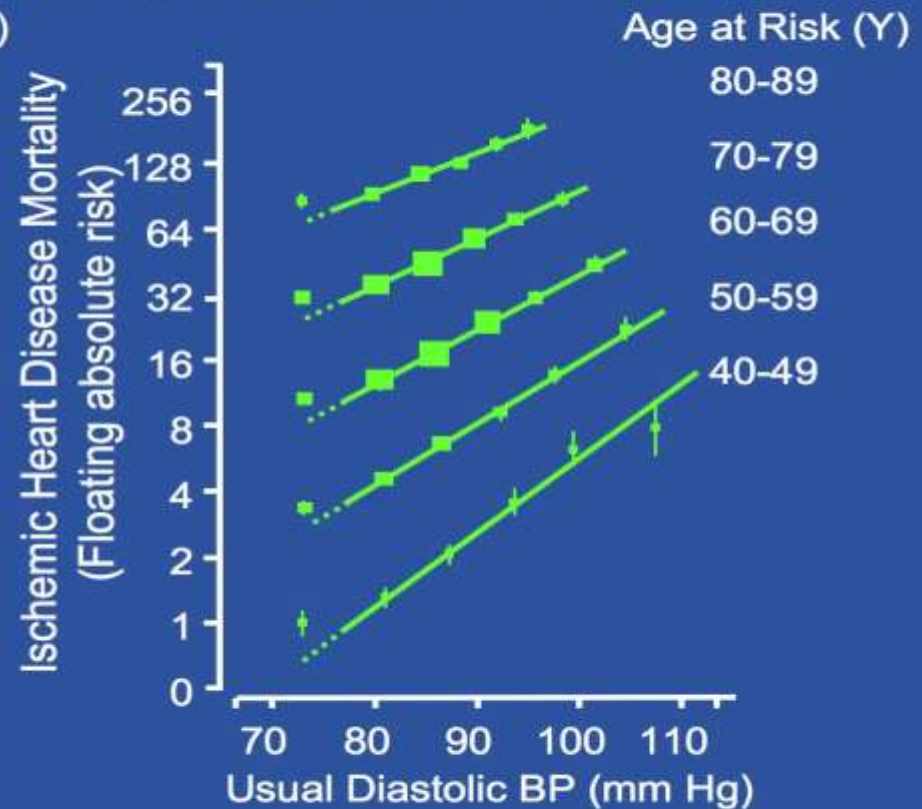
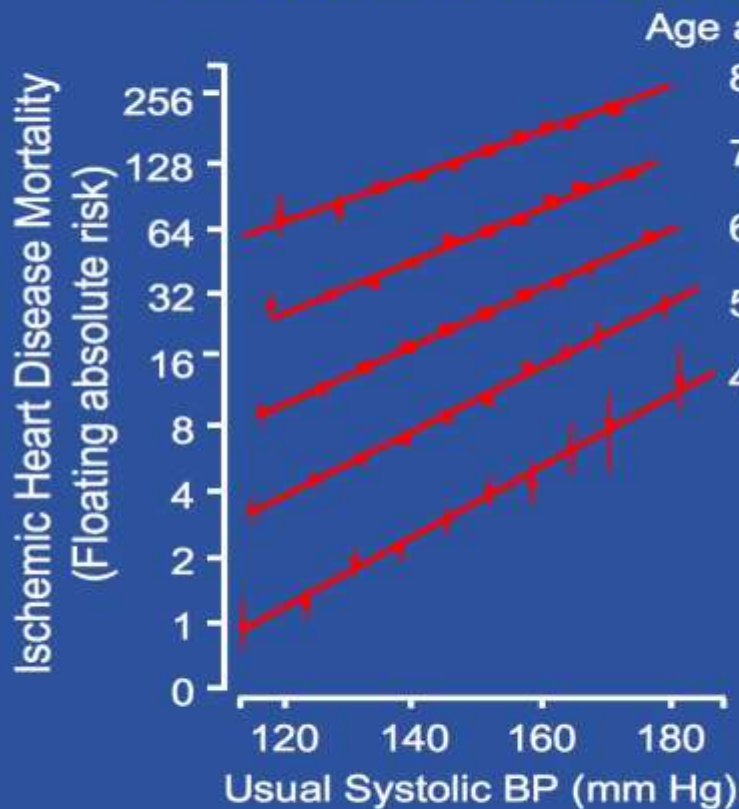


Hypertension defined as blood pressure $\geq 140/90$ mmHg or treatment

JNC-VI. *Arch Intern Med* 1997;157:2413-2446

Blood Pressure: Lower is Better

Ischemic Heart Disease Mortality and Blood Pressure

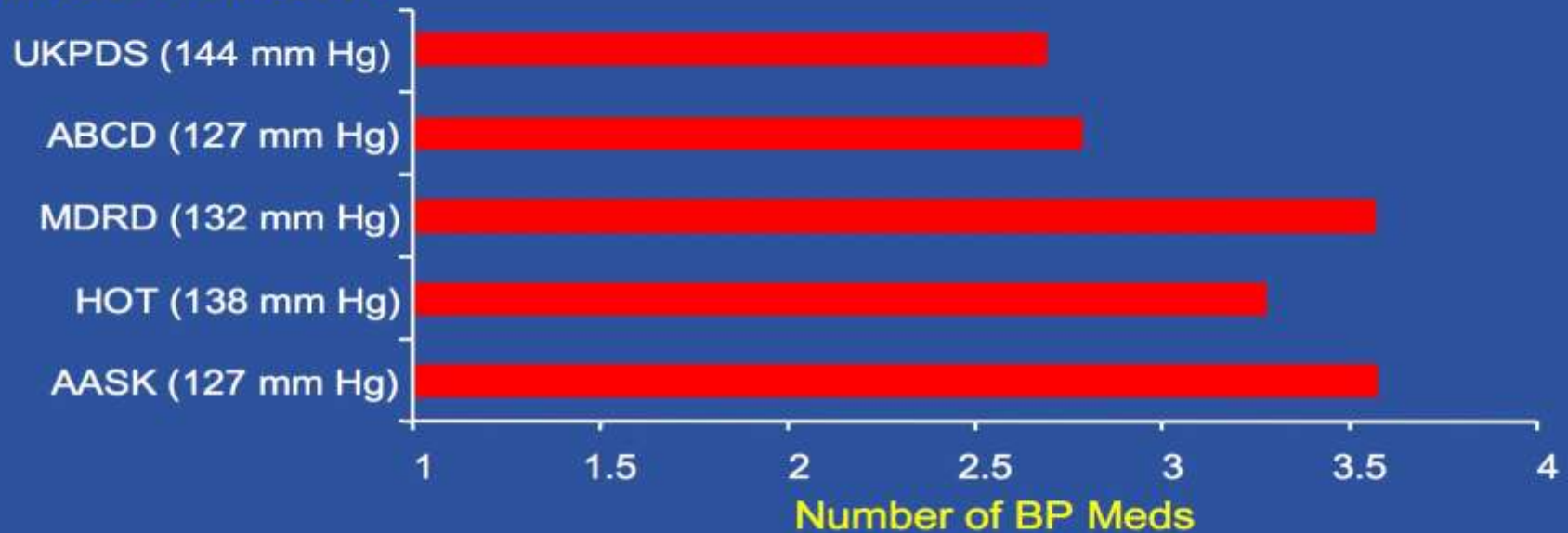


BP=Blood pressure

Prospective Studies Collaboration. *Lancet* 2002;360:1903-1913

Blood Pressure: Number of Medications Needed

Trial (SBP Achieved)



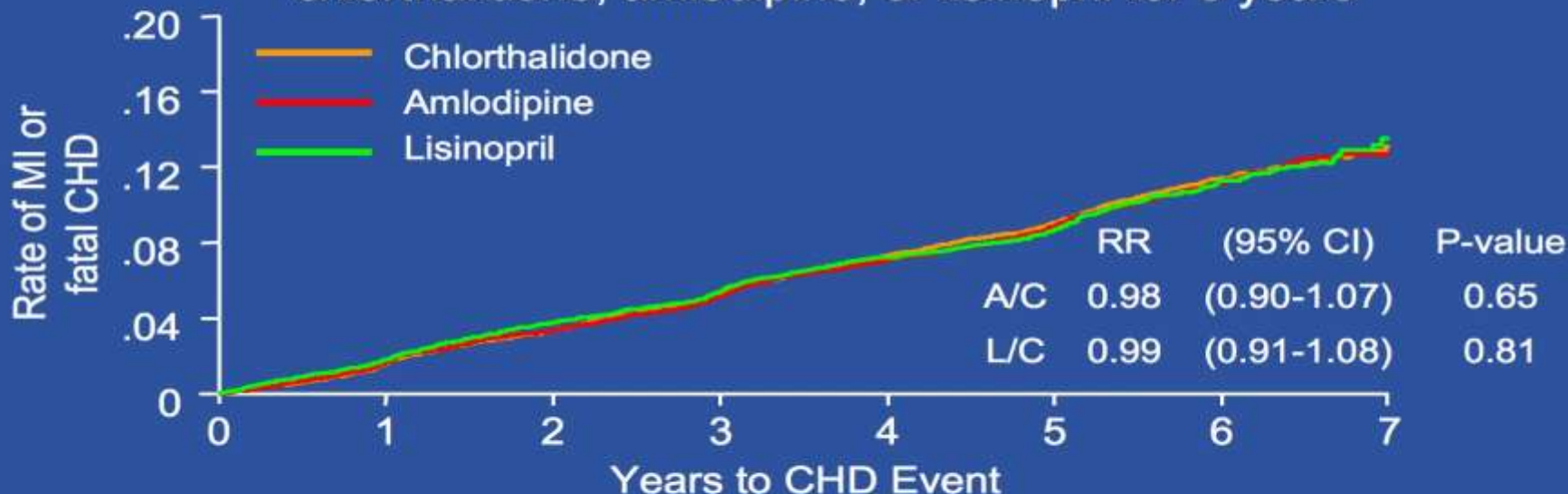
UKPDS=UK Prospective Diabetes Study;
ABCD=Appropriate Blood Pressure Control in Diabetes;
MDRD=Modification of Dietary Protein in Renal Disease;
HOT=Hypertension Optimal Treatment; AASK=African
American Study of Kidney Disease and Hypertension

Abbott K et al. *J Clin Pharmacology* 2004;44:431-438

Blood Pressure Evidence: Primary Prevention

Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)

33,357 patients with HTN and ≥ 1 CHD risk factor randomized to chlorthalidone, amlodipine, or lisinopril for 5 years



There is similar efficacy among BP lowering agents

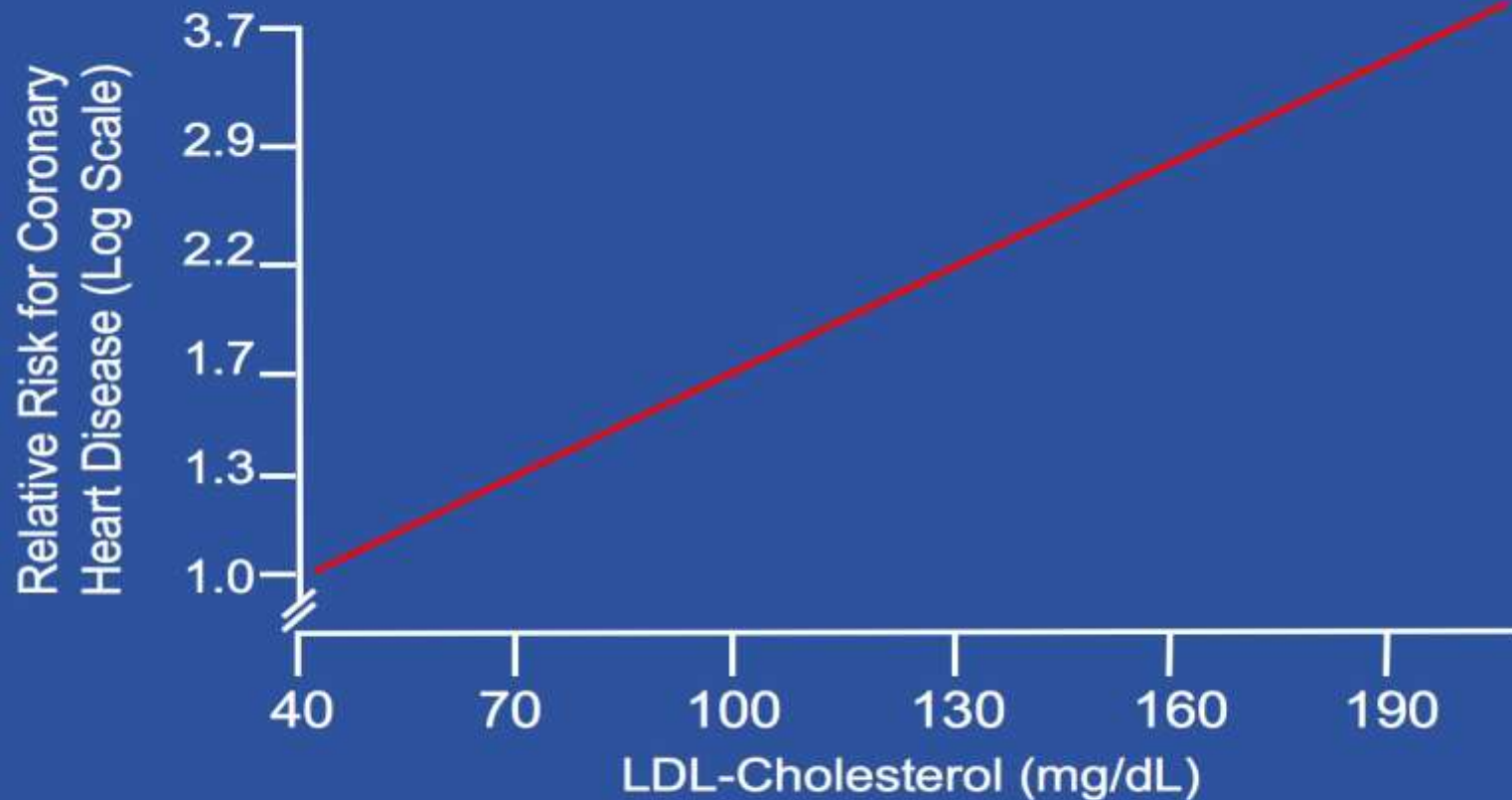
BP=Blood pressure, CHD=Coronary heart disease, HTN=Hypertension, MI=Myocardial infarction

ALLHAT Investigators. *JAMA* 2002;288:2981-97

Cholesterol Management Evidence



CHD Risk According to LDL-C Level



CHD=Coronary heart disease, LDL-C=Low-density lipoprotein cholesterol

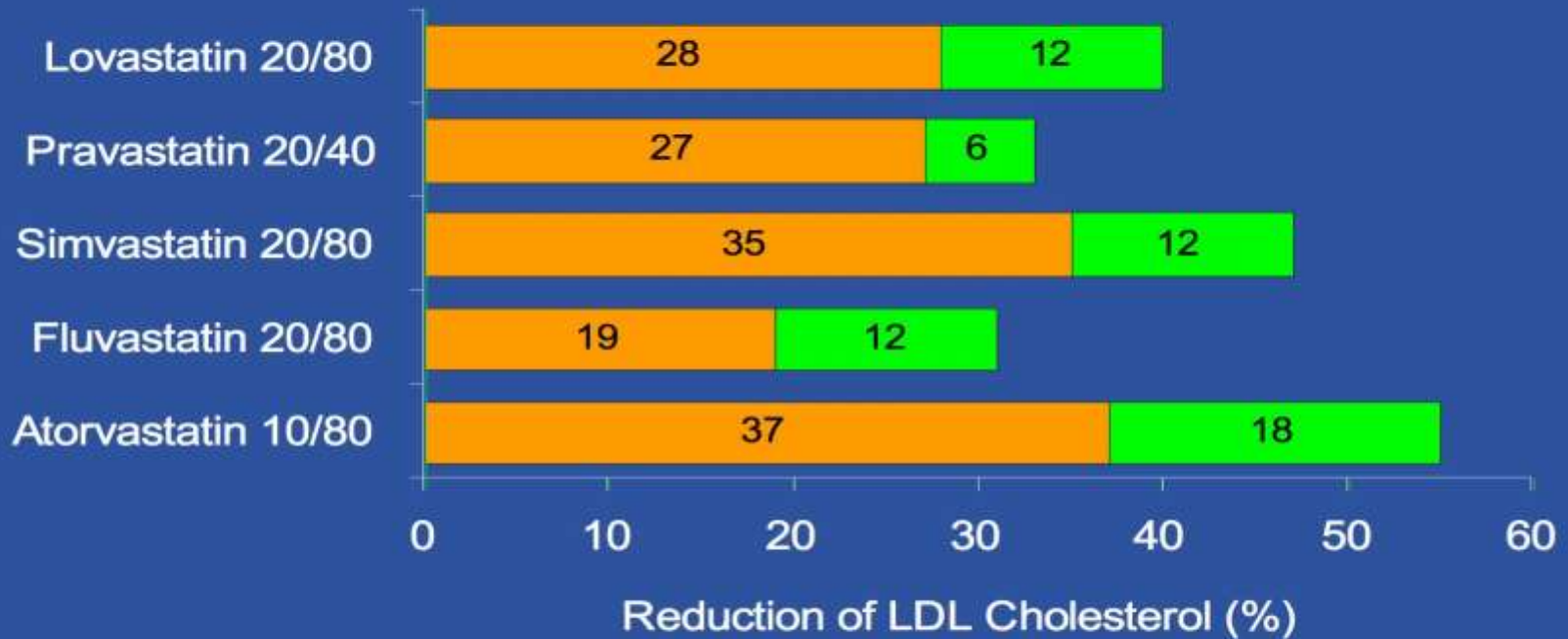
Grundy S et al. *Circulation* 2004;110:227-39

Therapies to Lower LDL-C

Class	Drug(s)
3-Hydroxy-3-Methylglutaryl Coenzyme A (HMG-CoA) reductase inhibitors [Statins]	Atorvastatin (Lipitor) Fluvastatin (Lescol XL) Lovastatin (generic and Mevacor) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor)
Bile acid sequestrants	Cholestyramine (generic and Questran) Colesevelam (Welchol) Colestipol (Colestid)
Cholesterol absorption inhibitor	Ezetimibe (Zetia)
Nicotinic acid	Niacin
Dietary Adjuncts	Soluble fiber Soy protein Stanol esters

HMG-CoA Reductase Inhibitor: Dose-Dependent Effect

The Rule of 6's



Each doubling of the statin dose produces an additional 6% (approximate) reduction in the LDL-C level

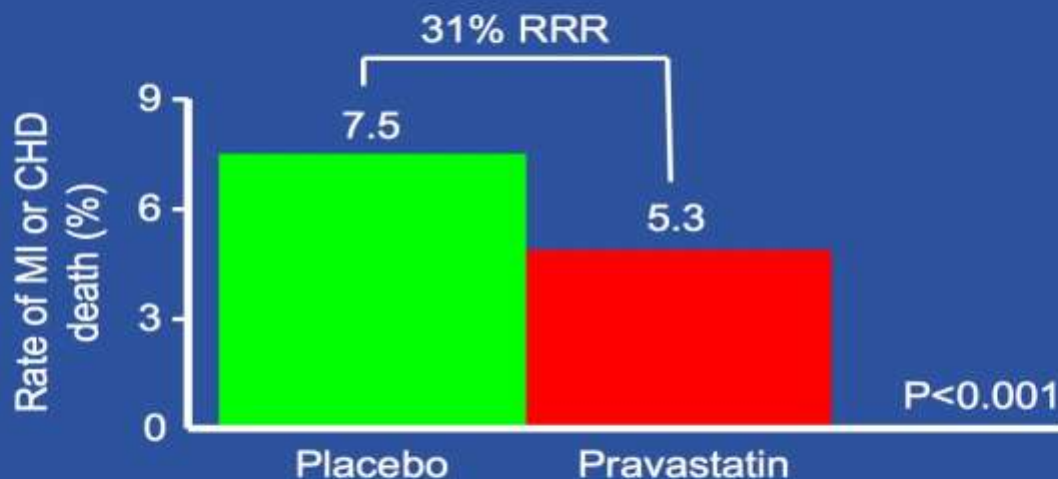
Illingworth DR. *Med Clin North Am* 2000;84:23-42

51

HMG-CoA Reductase Inhibitor: Primary Prevention

West of Scotland Coronary Prevention Study (WOSCOPS)

6,595 men with moderate hypercholesterolemia randomized to pravastatin (40 mg) or placebo for 5 years



Statins provide significant benefit in those with average cholesterol levels

CHD=Coronary heart disease, MI=Myocardial infarction,
RRR=Relative risk reduction

Shepherd J et al. *NEJM* 1995;333:1301-1307

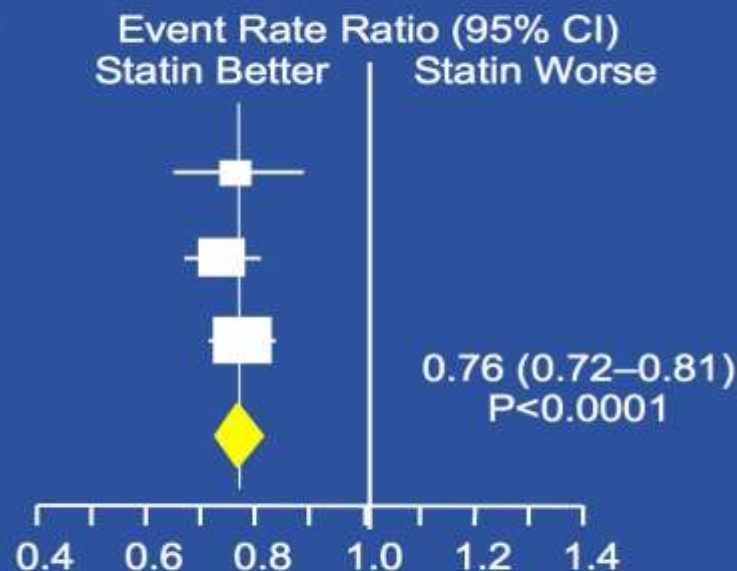
54

HMG-CoA Reductase Inhibitor: Secondary Prevention

Heart Protection Study (HPS)

20,536 patients with CAD, other occlusive arterial disease, or DM randomized to simvastatin (40 mg) or placebo for 5.5 years

Baseline	Statin	Placebo
LDL-C (mg/dL)	(n = 10,269)	(n = 10,267)
<100	282 (16.4%)	358 (21.0%)
100–129	668 (18.9%)	871 (24.7%)
≥130	1083 (21.6%)	1356 (26.9%)
All patients	2033 (19.8%)	2585 (25.2%)



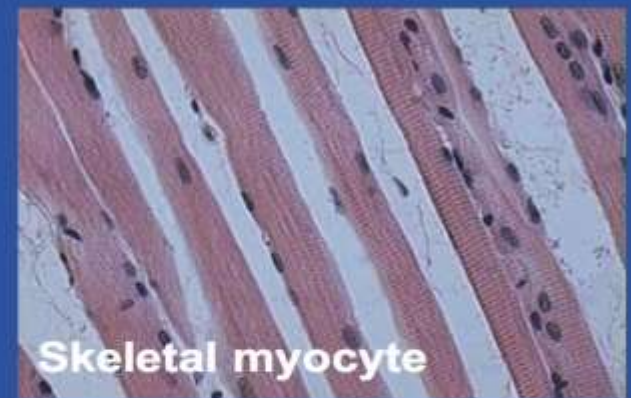
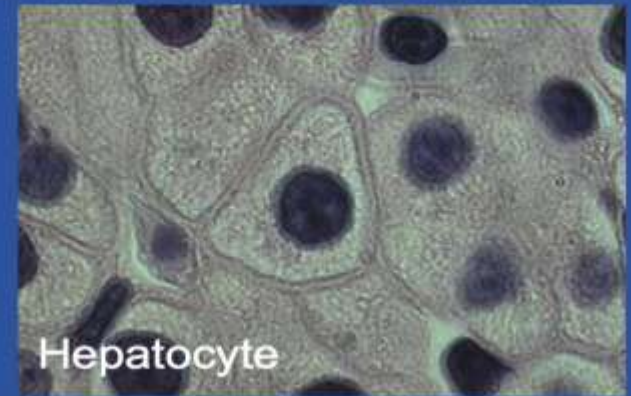
Statins provide significant benefit across a broad range of LDL-C levels

CAD=Coronary artery disease, CI=Confidence interval,
DM=Diabetes mellitus,

HPS Collaborative Group. *Lancet* 2002;360:7-22

HMG-CoA Reductase Inhibitor: Adverse Effects

- 0.5-2.0% incidence of elevated hepatic transaminases
- Dose-dependent phenomenon
- Usually reversible and rarely leads to progressive hepatic failure
- 5% incidence of myalgias (rare significant rise in CPK)
- 0.1% incidence of myositis (with CPK up to 10 times the upper limit of normal)
- 0.0001% incidence of fatal rhabdomyolysis.



Pasternak RC et al. Circulation 2002;106:1024-1028

70

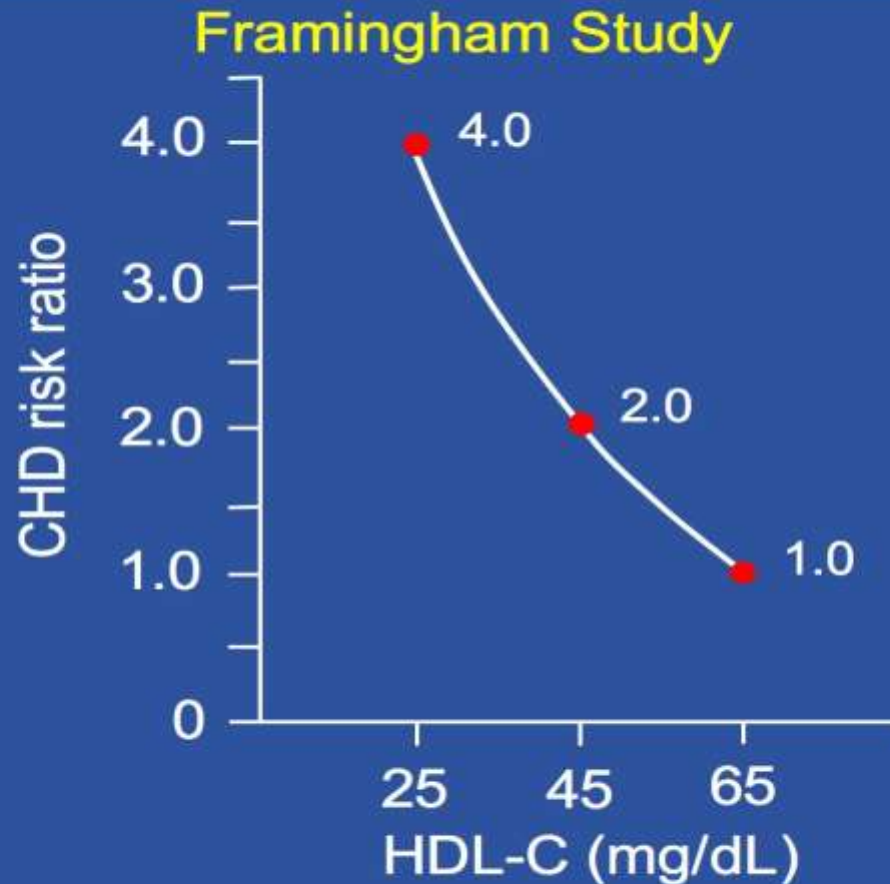
Dietary Adjuncts: Efficacy at Reducing LDL-C

Therapy	Dose (g/day)	Effect
Dietary soluble fiber	2-8	↓ LDL-C 5-10%
Soy protein	20-30	↓ LDL-C 5-7%
Stanol esters	1.5-4	↓ LDL-C 10-15%



Jones PJ. *Curr Atheroscler Rep* 1999;1:230-235
Lichtenstein AH. *Curr Atheroscler Rep* 1999;1:210-214
Rambjor GS et al. *Lipids* 1996;31:S45-S49
Ripsin CM et al. *JAMA* 1992;267:3317-3325

CHD Risk According to HDL-C Levels



CHD=Coronary heart disease, HDL-C=High-density lipoprotein cholesterol

Kannel WB. *Am J Cardiol* 1983;52:9B-12B

Cigarette Smoking Cessation Evidence



Smoking Prevalence in the United States



MMWR 1999;48:998
National Center for Health Statistics-1998

Cigarette Smoking Cessation: Evidence

Common preventable causes of death in U.S. in 1990 & 2000

Causes	# (%) in 1990	# (%) in 2000
Tobacco	400,000 (19)	435,000 (18)
Poor diet and physical activity (obesity)	300,000 (14)	400,000 (17)
Alcohol consumption	100,000 (5)	85,000 (4)
Microbial agents	90,000 (4)	75,000 (3)
Toxic agents	60,000 (3)	55,000 (2)
Motor vehicle accidents	25,000 (1)	43,000 (2)
Firearms	35,000 (2)	29,000 (1)
Sexual behavior	30,000 (1)	20,000 (<1)
Illicit drug use	20,000 (<1)	17,000 (<1)
Total	1,060,000 (50)	1,159,000 (48%)

Mokdad AH et al. *JAMA* 2004;291:1238-1245

92



mensHEALTH
INITIATIVE OF BC



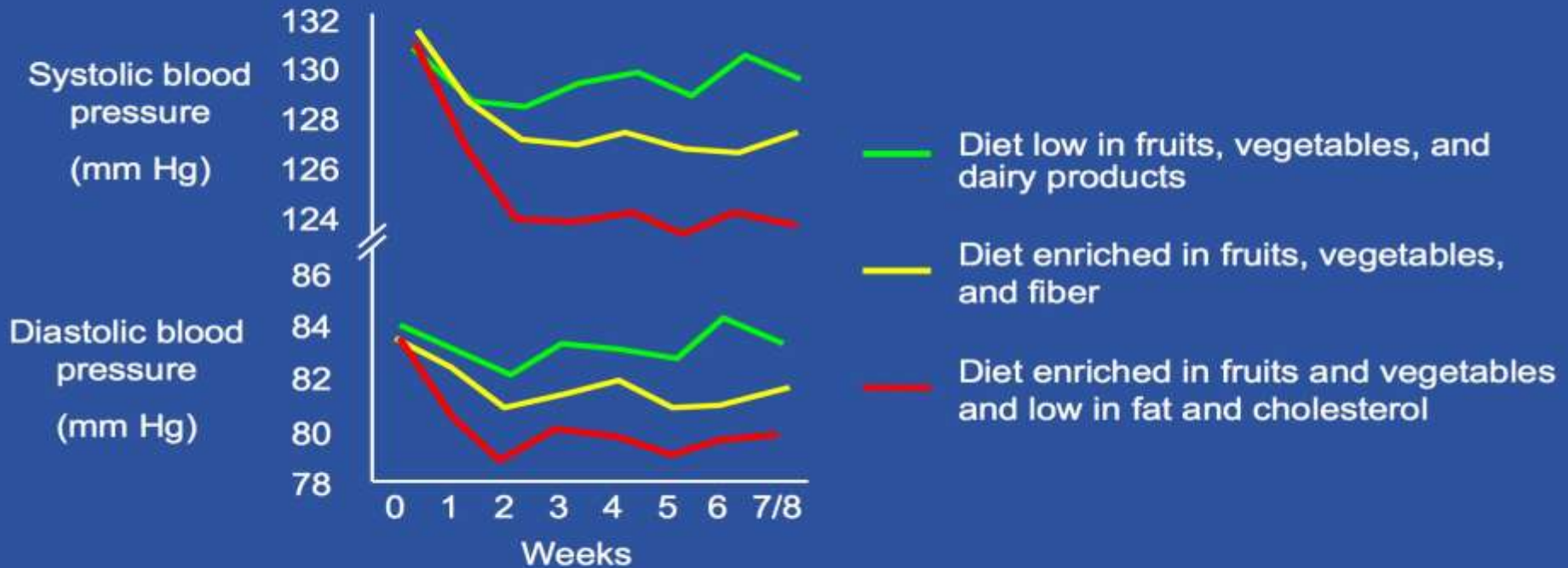
Diet and Weight Management Evidence



Diet Evidence: Effect on Blood Pressure

Dietary Approaches to Stop Hypertension (DASH) Group

459 hypertensive patients randomized to 1 of 3 diets for 8 weeks

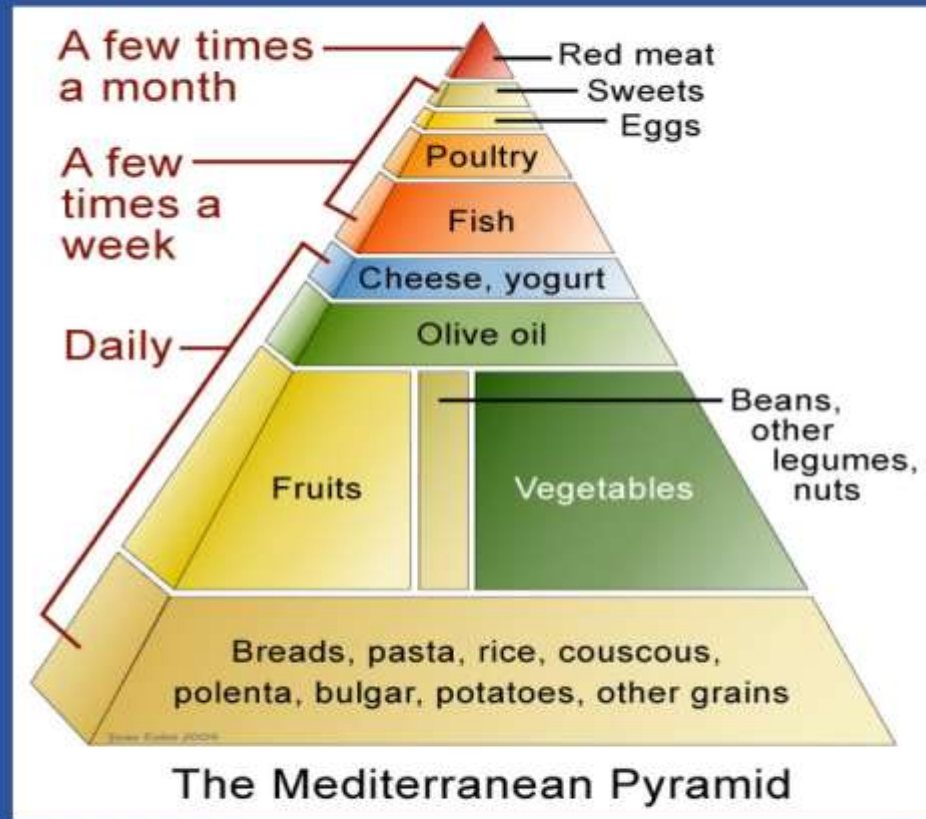
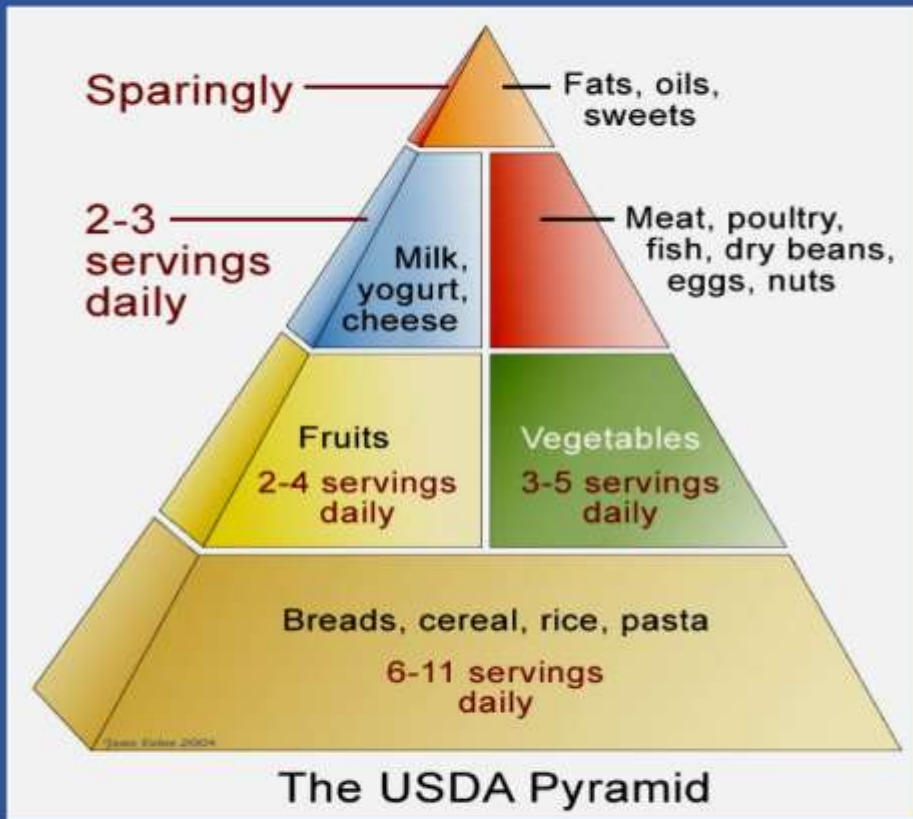


A diversified diet improves blood pressure

Appel LJ et al. *NEJM* 1997;336:1117-24

105

USDA vs. Mediterranean Dietary Recommendations

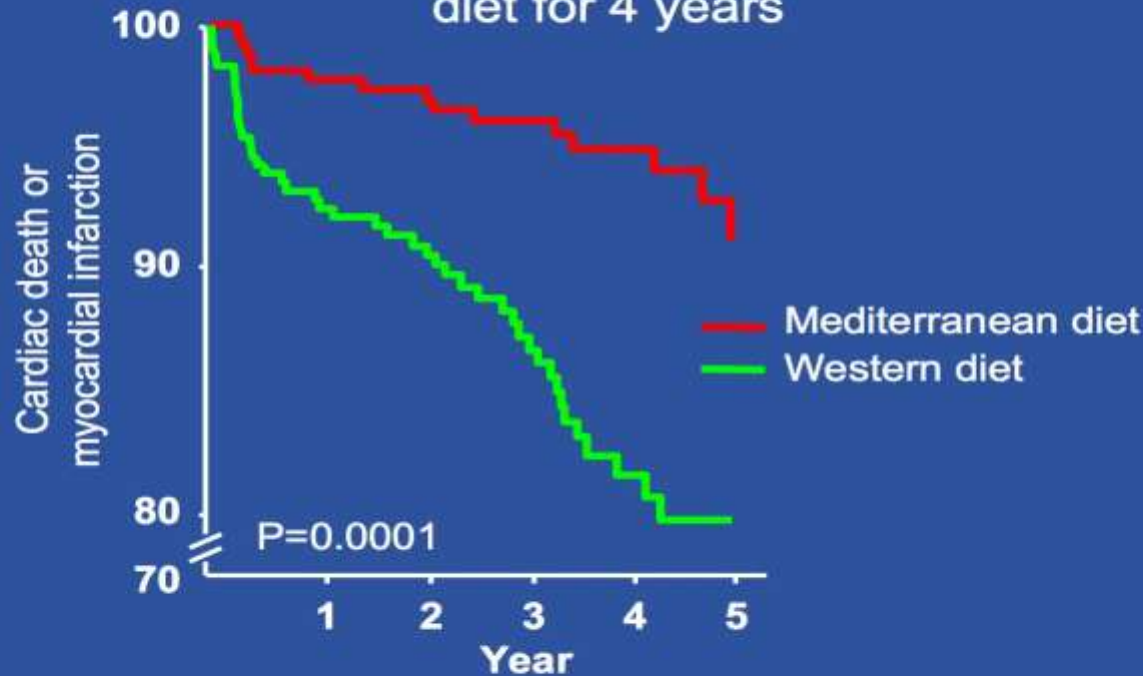


USDA=United States Department of Agriculture

Diet Evidence: Secondary Prevention

Lyon Diet Heart Study

605 patients following a MI randomized to a Mediterranean* or Western** diet for 4 years



A “Mediterranean” diet reduces CVD event rates

*High in polyunsaturated fat and fiber

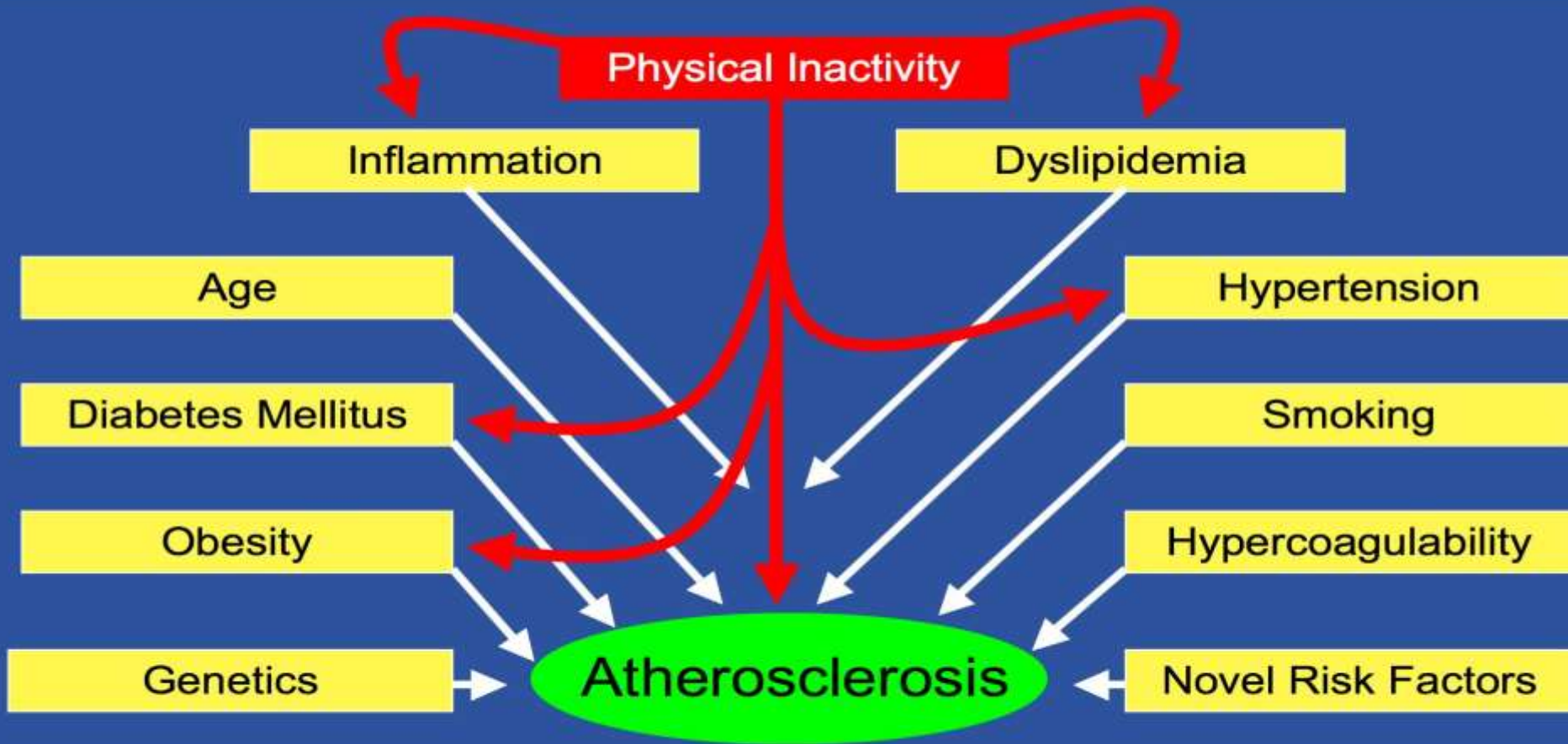
**High in saturated fat and low in fiber

De Lorgeril M et al. *Circulation* 1999;99:779-785

Exercise Evidence

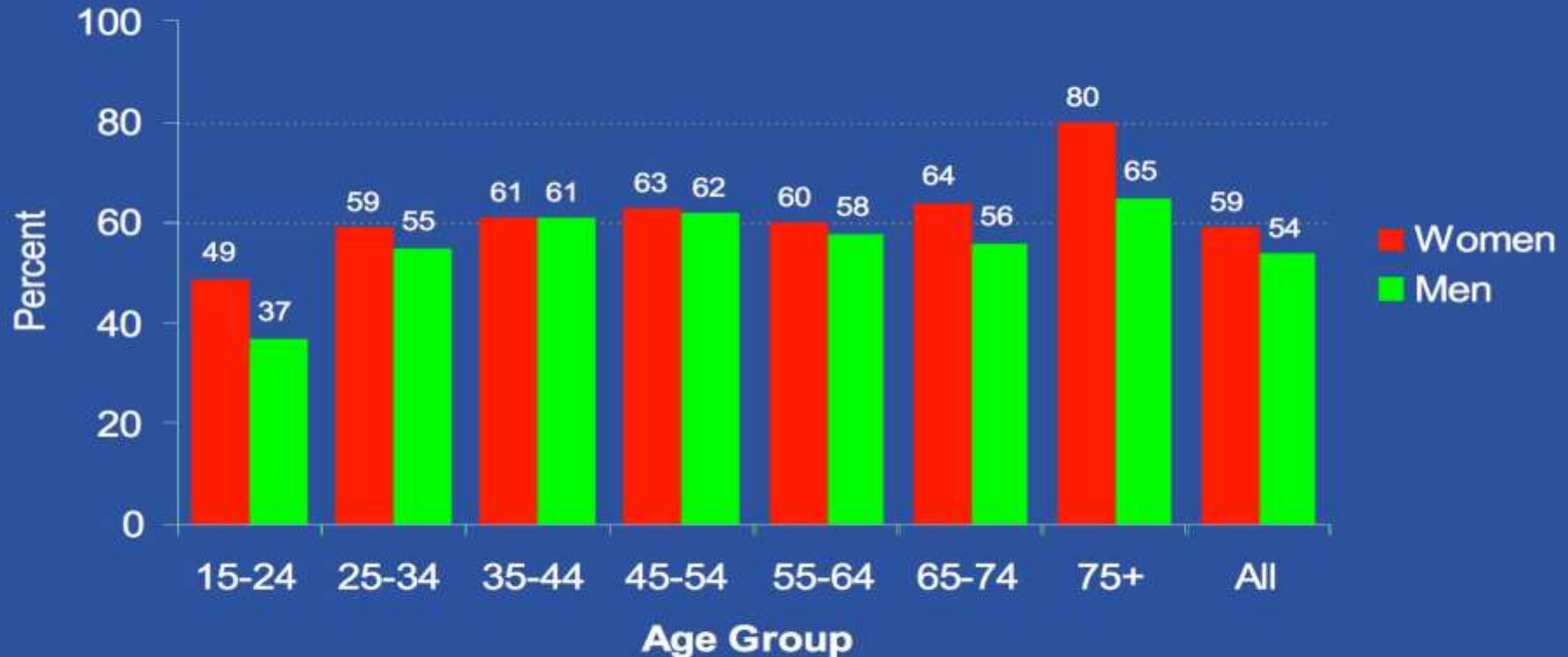


Exercise Evidence: Role of Physical Inactivity



Prevalence of Physical Inactivity

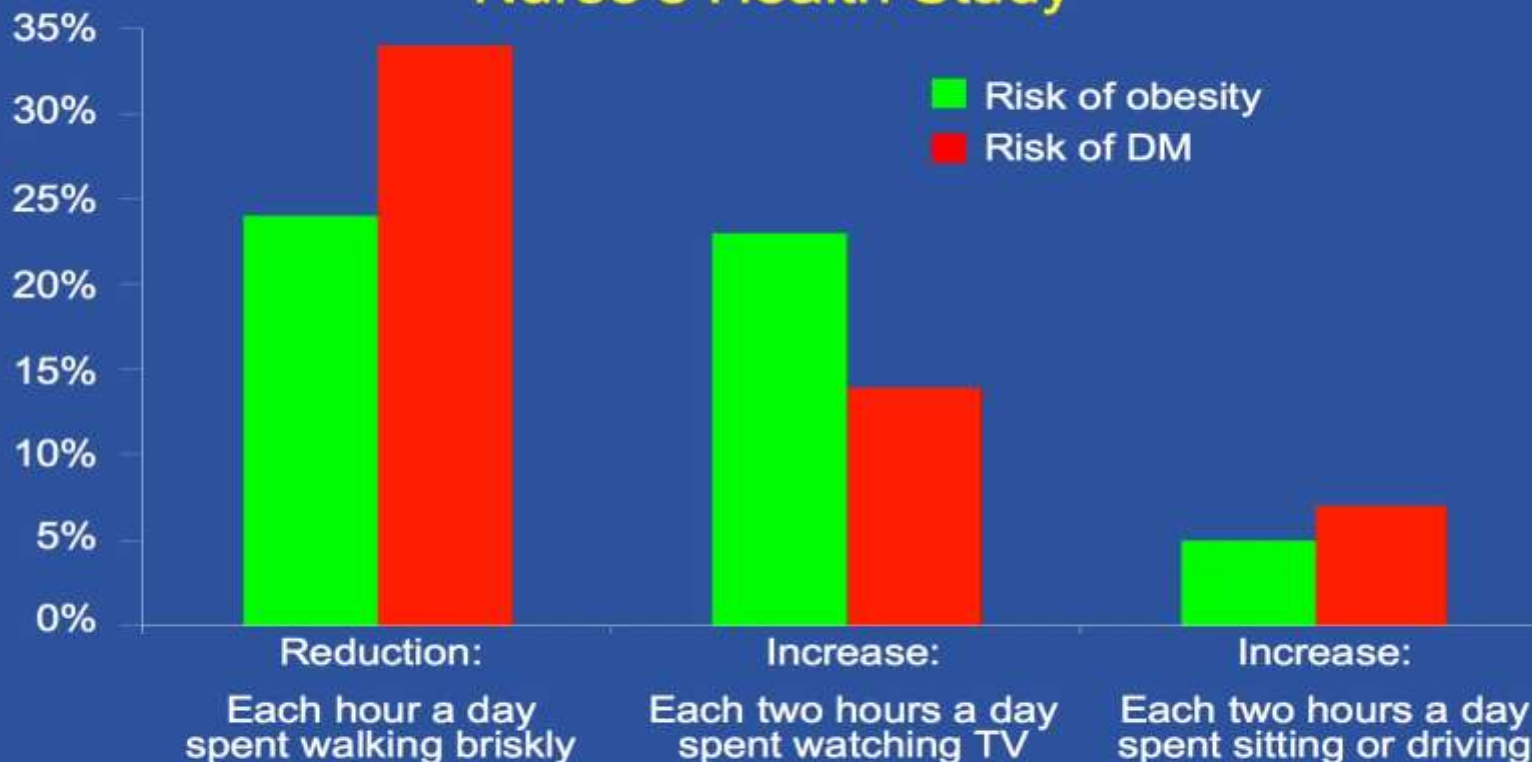
National Population Health Survey



Statistics Canada, National Population Health Survey, 1996/1997

Exercise Evidence: Effect on Obesity and Diabetes

Nurse's Health Study



Exercise reduces the incidence of obesity and DM

DM=Diabetes mellitus

Hu FB et al. *JAMA* 2003;289:1785-91

141

Influenza Vaccination Evidence



Influenza Vaccination: Primary Prevention

286,383 community-dwelling members aged ≥ 65 years of 3 large managed-care organizations evaluated for 1-2 yrs

Adverse Outcome	Vaccinated Subjects (N=77,738)	Unvaccinated Subjects (N=62,317)	Adjusted Odds Ratio	P value
Hospitalization for CHD	457 (0.6)	535 (0.9)	0.80	0.001
Hospitalization for HF	466 (0.6)	538 (0.9)	0.81	0.002
Hospitalization for CVD	398 (0.5)	427 (0.7)	0.84	0.018
Death	943 (1.2)	1361 (2.2)	0.52	<0.001
Hospitalization or death	2387 (3.1)	2910 (4.7)	0.65	<0.001

Influenza vaccination reduces adverse CV events

Nichol KL et al. *NEJM* 2003;348:1322-32

147

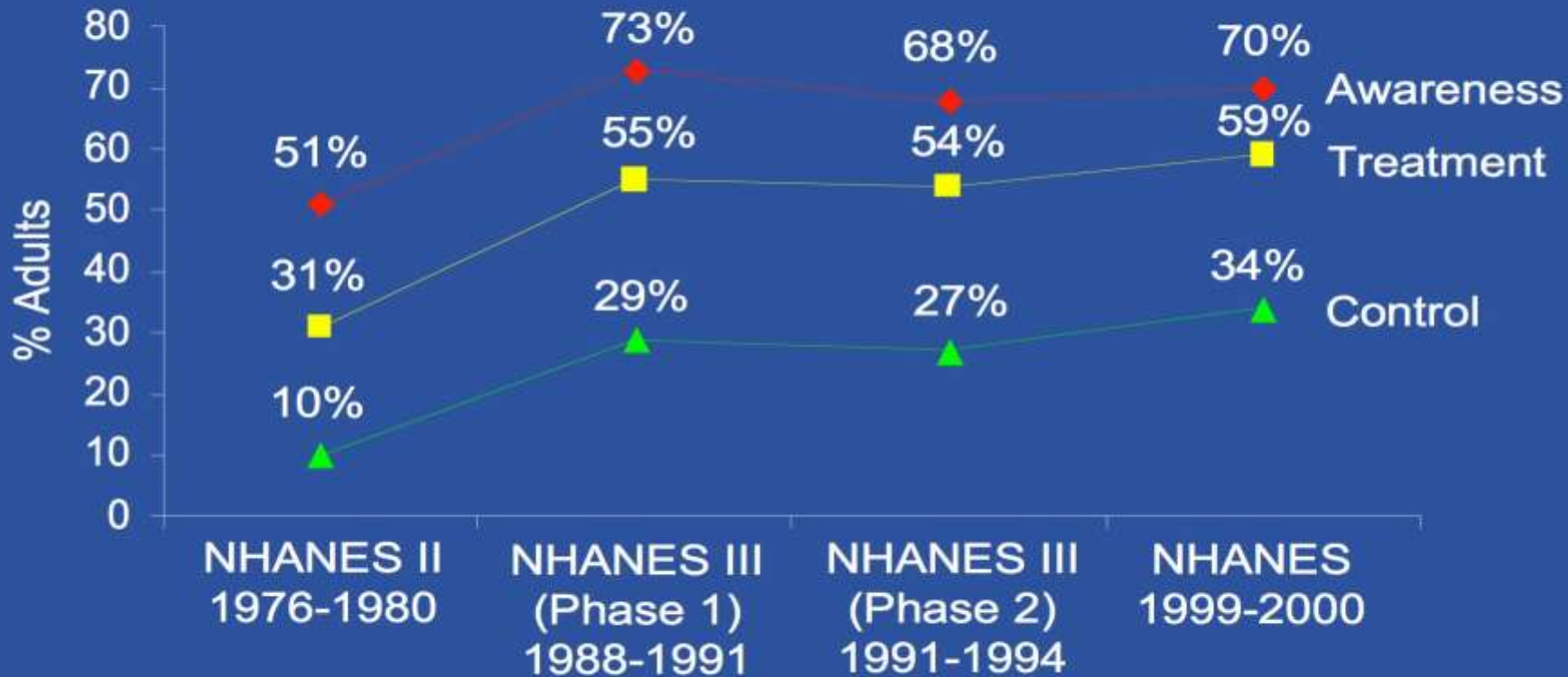


mensHEALTH
INITIATIVE OF BC



U.S. Hypertension Awareness, Treatment, and Control

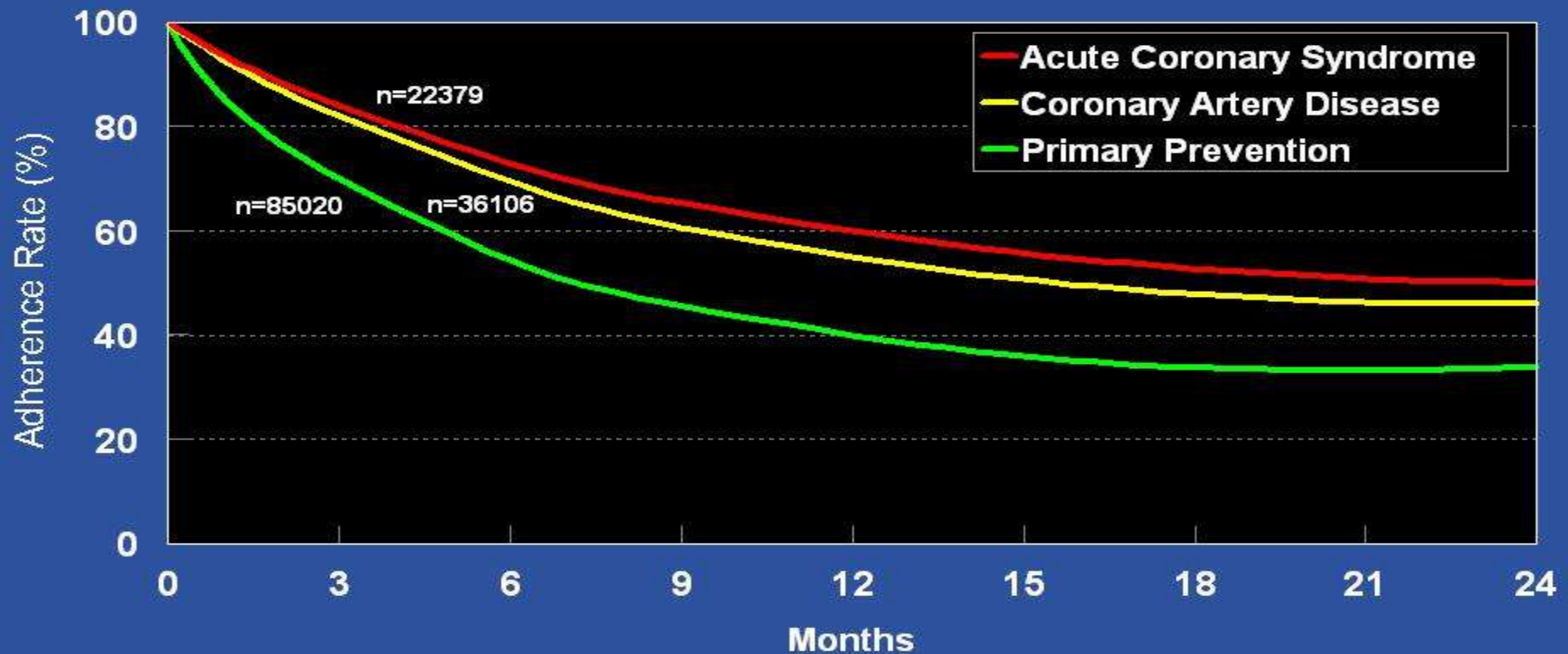
National Health and Nutrition Examination Survey (NHANES)



Chobanian AV et al. *JAMA* 2003;289:2560-2572

165

Adherence Rates to HMG-coA Reductase Inhibitors



Jackevicius CA et al. *JAMA* 2002;288:462-467