



UNIVERSITY OF
SASKATCHEWAN



BP, LDL, BS... SOS
A CV risk update

David Blackburn

Associate Professor

College of Pharmacy & Nutrition



UNIVERSITY OF
SASKATCHEWAN



Quick updates

YOU DECIDE WHERE WE START

- **Blood pressure - Slide #3**
- **Cholesterol -- Slide # 17**



UNIVERSITY OF
SASKATCHEWAN



Hypertension



Hypertension -- the good news

66% treated and controlled in 2006

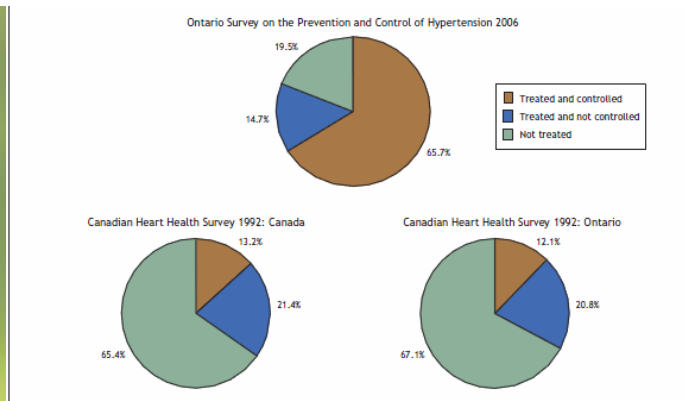
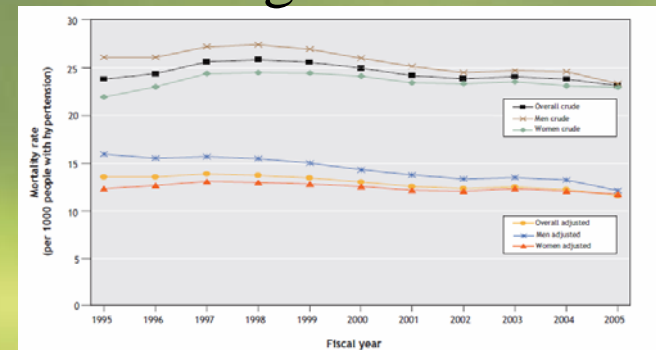


Figure 2: Treatment and control of hypertension as determined in 2006 by the Ontario Survey on the Prevalence and Control of Hypertension and in 1992, for Ontario and Canada as a whole, in the Canadian Heart Health Survey (1992 data supplied by Dr. Michel Joffres, Simon Fraser University, personal communication, July 31, 2007). The data are presented as percentage of the population with diagnosed hypertension. Both sets of Ontario data were weighted to the Ontario population, and the national data were weighted to the Canadian population. For consistency of comparison, "treatment" in the Canadian Heart Health Survey refers to drug therapy only.

Leenen et al. CMAJ 2008;
178: 1441-1449

Mortality appears to be decreasing

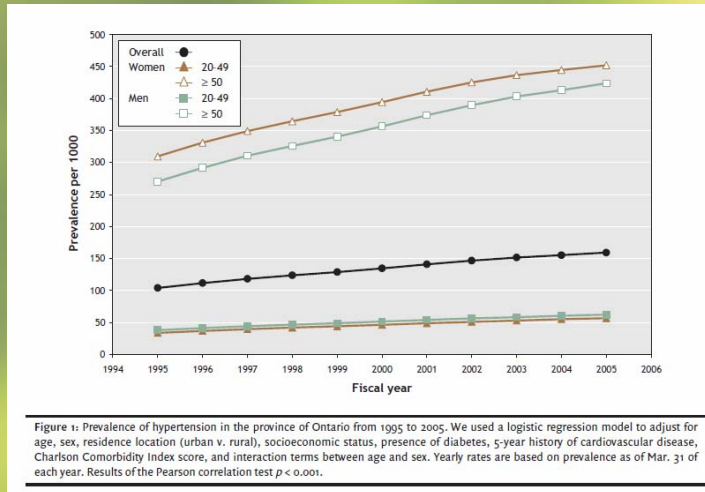


Tu et al. CMAJ 2008;
178: 1436 - 1440



Hypertension -- the bad news

Prevalence of HTN is increasing quickly



- Lots of work ahead !

Tu et al. CMAJ 2008;
178: 1429-1435



UNIVERSITY OF
SASKATCHEWAN



Hypertension --- the drugs



Beta-blockers in hypertension Continue to get beaten up!!

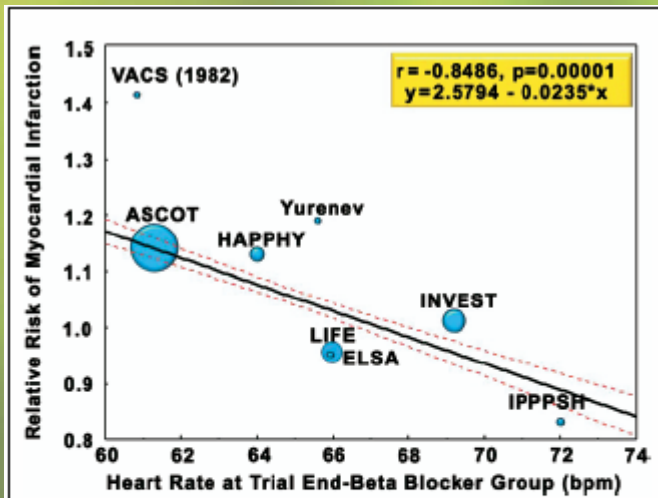


Figure 3 Risk of Nonfatal MI as Function of Heart Rate

Relative risk of nonfatal myocardial infarction (MI) as a function of heart rate achieved at the end of the study in the beta-blocker group. The **diameter of the circles** represents the weight of each individual trial. The **line** represents the regression fit with 95% confidence interval for the effect sizes. VACS – Veterans Administration Cooperative Study Group on Antihypertensive Agents; other abbreviations as in Figure 2.

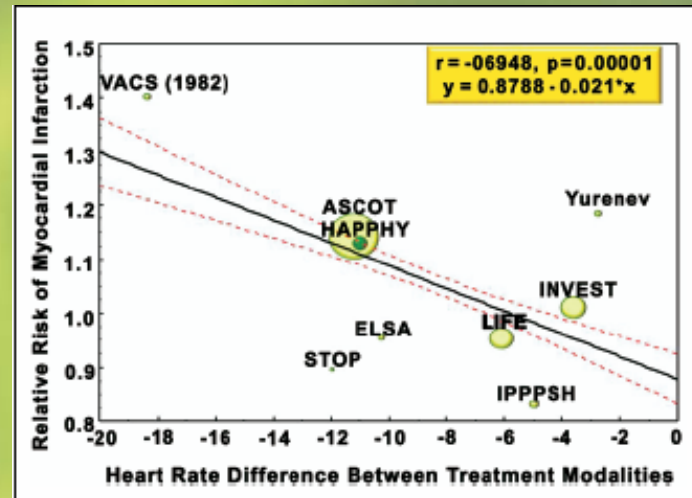
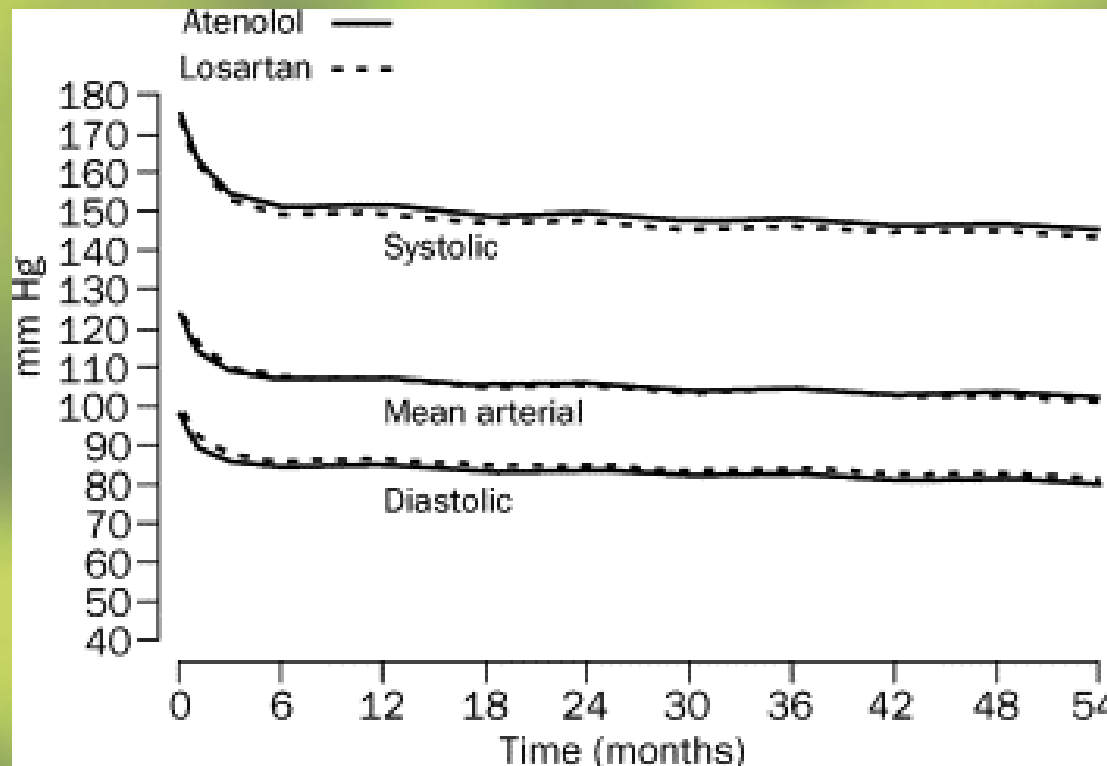


Figure 4 Risk of Nonfatal MI as Function of Heart Rate Difference Between Treatments

Relative risk of nonfatal MI as a function of heart rate difference between treatment modalities. The **diameter of the circles** represents the weight of each individual trial. The **line** represents the regression fit with 95% confidence interval for the effect sizes. STOP – Swedish Trial in Old Patients With Hypertension; other abbreviations as in Figure 2.



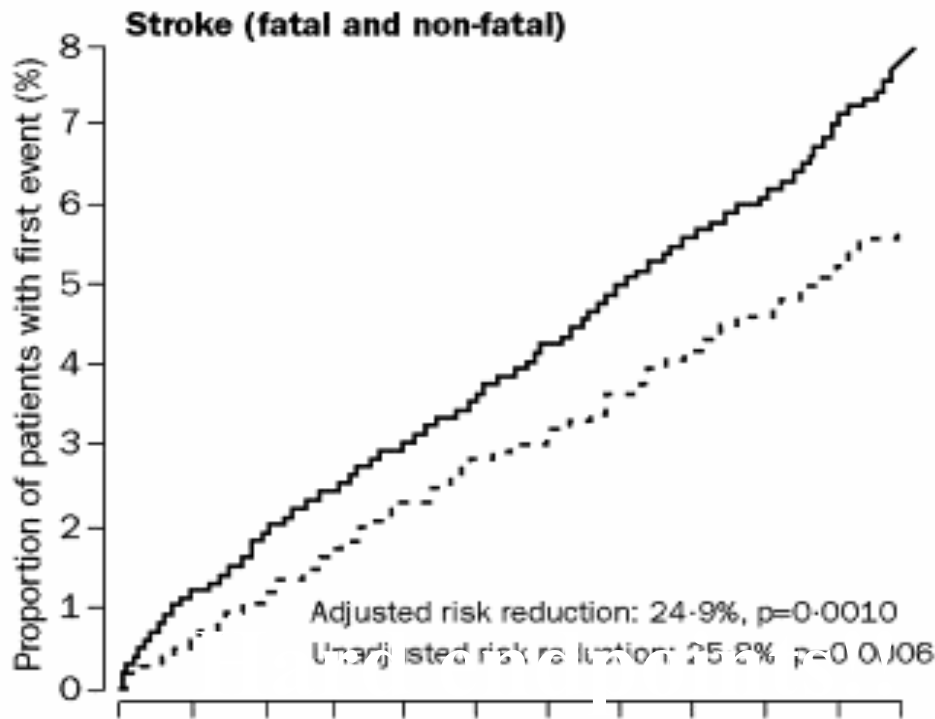
Remember the LIFE study?



Dahlof et al. Lancet
2002; 359:995-1003



Despite identical blood pressure...



Dahlof et al. Lancet 2002; 359:995-1003



Beta-blockers in HTN

- **Only useful in patients with**
 - **Systolic heart failure**
 - **Atrial fibrillation**
 - **Hypertension AND recent heart attack / Acute coronary syndrome**
 - **High heart rates (?)**
- **Other blood pressure medications likely provide better protection against hypertension-related injury**



UNIVERSITY OF
SASKATCHEWAN



Combinations of hypertensive drugs



UNIVERSITY OF
SASKATCHEWAN



The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

DECEMBER 4, 2008

VOL. 359 NO. 23

Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk Patients

Kenneth Jamerson, M.D., Michael A. Weber, M.D., George L. Bakris, M.D., Björn Dahlöf, M.D., Bertram Pitt, M.D., Victor Shi, M.D., Allen Hester, Ph.D., Jitendra Gupte, M.S., Marjorie Gatlin, M.D., and Eric J. Velazquez, M.D.,
for the ACCOMPLISH trial investigators*

ABSTRACT

BACKGROUND

The optimal combination drug therapy for hypertension is not established, although current U.S. guidelines recommend inclusion of a diuretic. We hypothesized that treatment with the combination of an angiotensin-converting-enzyme (ACE) inhibitor and a dihydropyridine calcium-channel blocker would be more effective in reducing the rate of cardiovascular events than treatment with an ACE inhibitor plus a thiaz-

From the University of Michigan Health System, Ann Arbor (K.J., B.P.); the State University of New York Downstate Medical College, Brooklyn (M.A.W.); the University of Chicago Pritzker School of Medicine, Chicago (G.L.B.); Sahlgrenska University Hospital, Gothenburg, Sweden



High risk patients with hypertension

- Previous MI, kidney disease, LVH, or diabetes



All received benazepril (ACEI)

Amlodipine (CCB)
(n=5,744)

Hydrochlorothiazide
(n=5,762)



ACEI + CCB in high risk patients!

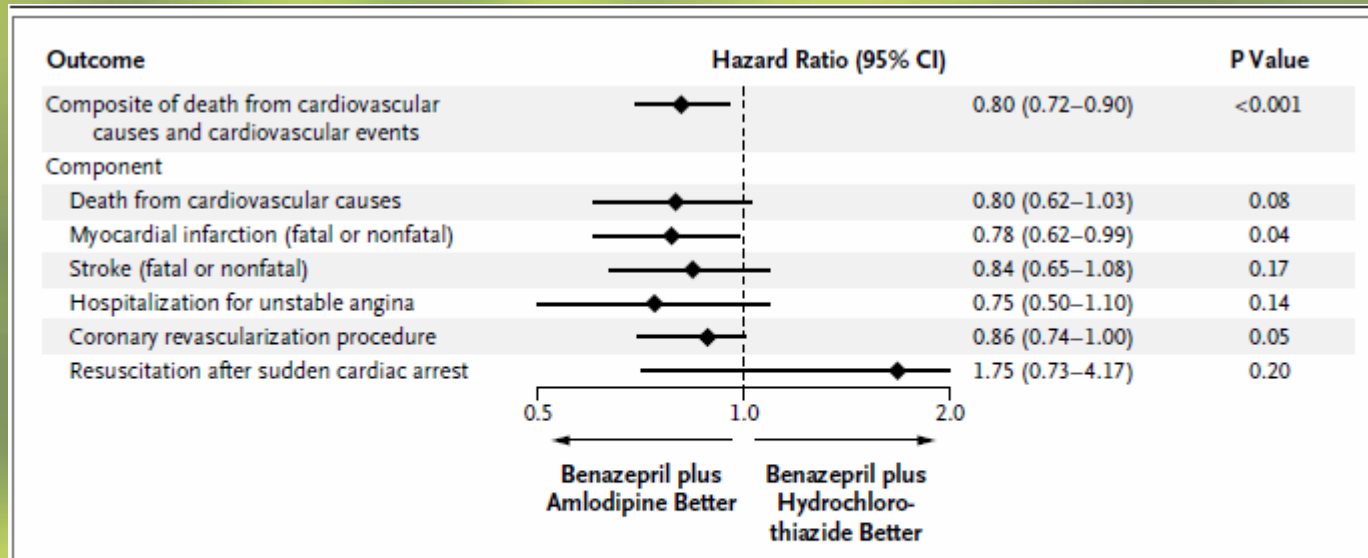
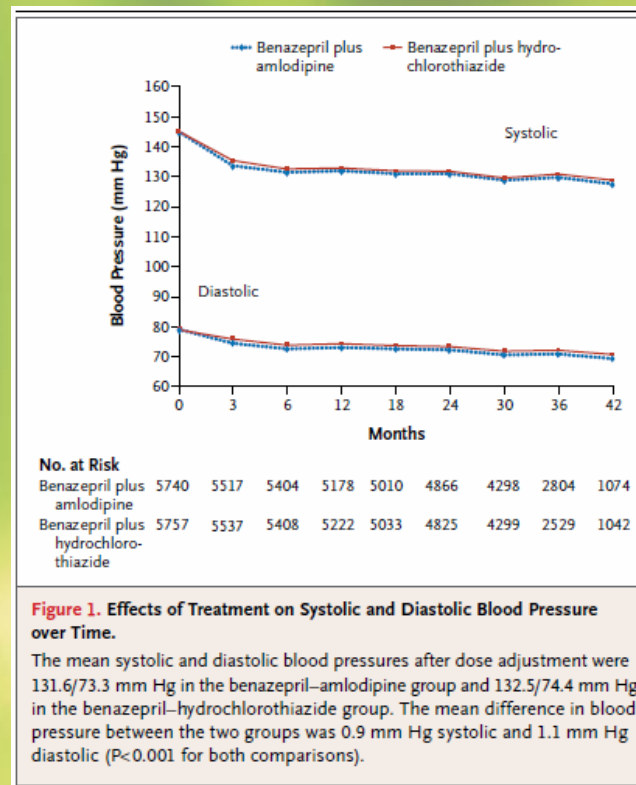


Figure 3. Hazard Ratios for the Primary Outcome and the Individual Components.

Only the first event in an individual patient was counted in the analysis of the primary end point. For the subsequent analysis of the component end points, if a patient had events in more than one category, one event per category was counted.



Differences **NOT** due to BP control



Jammerson et al. N Engl J Med 2008;359:2417-28
(ACCOMPLISH study)



Why was this combo better??

- **Amlodipine good ?**
- **HCTZ bad ? (what if chlorthalidone was used)**
- **Is there some synergy with this specific combo?**
- **Where would amlodipine + HCTZ fit??**
- **Where do beta-blockers fit in the high risk, hypertensive patient?**



UNIVERSITY OF
SASKATCHEWAN



Cholesterol -- new guidelines



SPECIAL ARTICLE

2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult – 2009 recommendations

Jacques Genest MD¹, Ruth McPherson MD PhD², Jiri Frohlich MD³, Todd Anderson MD⁴, Norm Campbell MD⁴, André Carpentier MD⁵, Patrick Couture MD⁶, Robert Dufour MD⁷, George Fodor MD², Gordon A Francis MD³, Steven Grover MD¹, Milan Gupta MD⁸, Robert A Hegele MD⁹, David C Lau MD¹⁰, Lawrence Leiter MD¹¹, Gary F Lewis MD¹², Eva Lonn MD¹³, GB John Mancini MD¹⁴, Dominic Ng MD PhD¹¹, Glen J Pearson PharmD¹⁵, Allan Sniderman MD¹⁶, James A Stone MD PhD¹⁰, Ehud Ur MD¹⁴

J Genest, R McPherson, J Frohlich, et al. 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult – 2009 recommendations. *Can J Cardiol* 2009;25(10): 567-579.

The present article represents the 2009 update of the Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult.

Les lignes directrices canadiennes 2009 de la Société canadienne de cardiologie pour le diagnostic et le traitement de la dyslipidémie ainsi que pour la prévention des maladies cardiovasculaires chez l'adulte – Des recommandations pour 2009

Le présent article contient la mise à jour 2009 des lignes directrices de la Société canadienne de cardiologie pour le diagnostic et le traitement de la dyslipidémie et pour la prévention des maladies cardiovasculaires chez l'adulte.



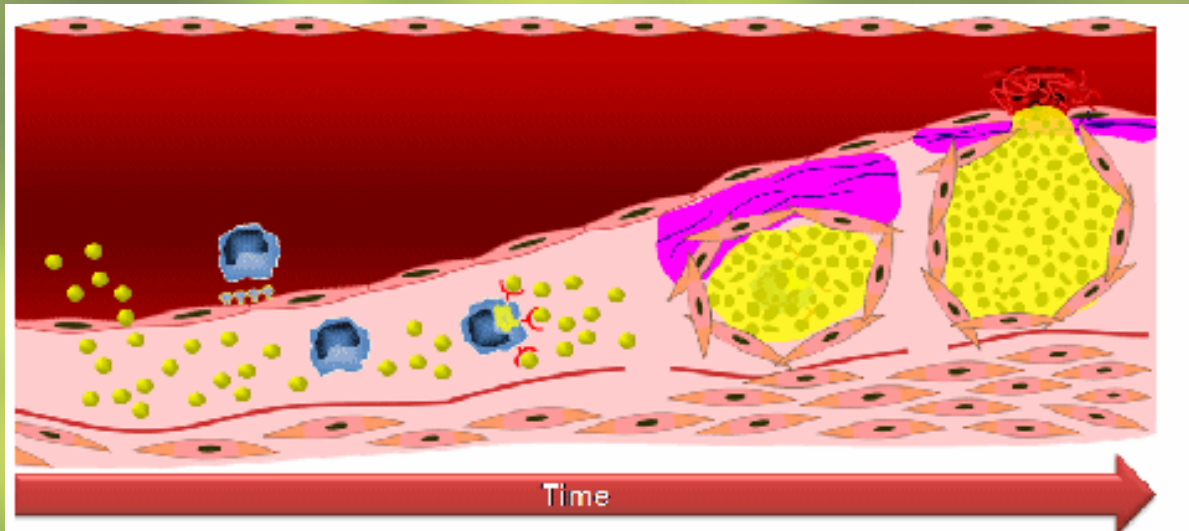
TABLE 3
Target lipid levels

Risk level	Initiate treatment if:	Primary targets	
		LDL-C	Alternate
High CAD, PVD, atherosclerosis* Most patients with diabetes FRS $\geq 20\%$ RRS $\geq 20\%$	Consider treatment in all patients	<2 mmol/L or $\geq 50\%$ \downarrow LDL-C Class I, level A	apoB <0.80 g/L Class I, level A
Moderate FRS 10%–19%	LDL-C >3.5 mmol/L TC/HDL-C >5.0 hs-CRP >2 mg/L Men >50 years Women >60 years Family history and hs-CRP modulates risk (RRS)	<2 mmol/L or $\geq 50\%$ \downarrow LDL-C Class IIa, level A	apoB <0.80 g/L Class IIa, level A
Low FRS <10%	LDL-C ≥ 5.0 mmol/L	$\geq 50\%$ \downarrow LDL-C Class IIa, level A	



Cholesterol guidelines – key points

- Importance of inflammation → CRP
 - Intermediate risk adults (>50 ♀ / >60 ♂) can be “promoted”





Cholesterol guidelines – key points

- **Goal**
 - LDL < 2.0mmol/L OR 50% reduction
- **Which target should you choose??**
 - 50% reduction in LDL – achievable and effective with statin
 - LDL < 2.0mmol/L – may require another drug?
- **Which drug to add to the statin??**
 - Ezetimibe or Niacin ?
- **Fibrates?**
 - Primarily for high triglycerides
 - Have had a “hard five years”



UNIVERSITY OF
SASKATCHEWAN



The NEW ENGLAND JOURNAL *of* MEDICINE

Extended-Release Niacin or Ezetimibe and Carotid Intima–Media Thickness

Allen J. Taylor, M.D., Todd C. Villines, M.D., Eric J. Stanek, Pharm.D., Patrick J. Devine, M.D., Len Griffen, M.D.,
Michael Miller, M.D., Neil J. Weissman, M.D., and Mark Turco, M.D.

ABSTRACT

BACKGROUND

Treatment added to statin monotherapy to further modify the lipid profile may include combination therapy to either raise the high-density lipoprotein (HDL) cholesterol level or further lower the low-density lipoprotein (LDL) cholesterol level.

METHODS

We enrolled patients who had coronary heart disease or a coronary heart disease risk

From the Cardiology Service, Walter Reed Army Medical Center (A.J.T., T.C.V., P.J.D., M.M.); and Medstar Research Institute, Washington Hospital Center (A.J.T., N.J.W.) — both in Washington, DC; Medco Health Solutions, Franklin Lakes, NJ (E.J.S.); Cardio Associates, Rockville, MD (L.G.); and

Taylor et al. N Engl J Med 2009;361



Patients

- **Adults**
- **High risk (either of the following)**
 - **CHD (prior MI or documented atherosclerosis)**
 - **High risk Framingham score**
 - **Diabetes**
- **Treated with a statin AND**
 - **LDL < 2.6mmol/L**
 - **HDL < 1.3 (< 1.4 ♀)**



Differing effects on cholesterol

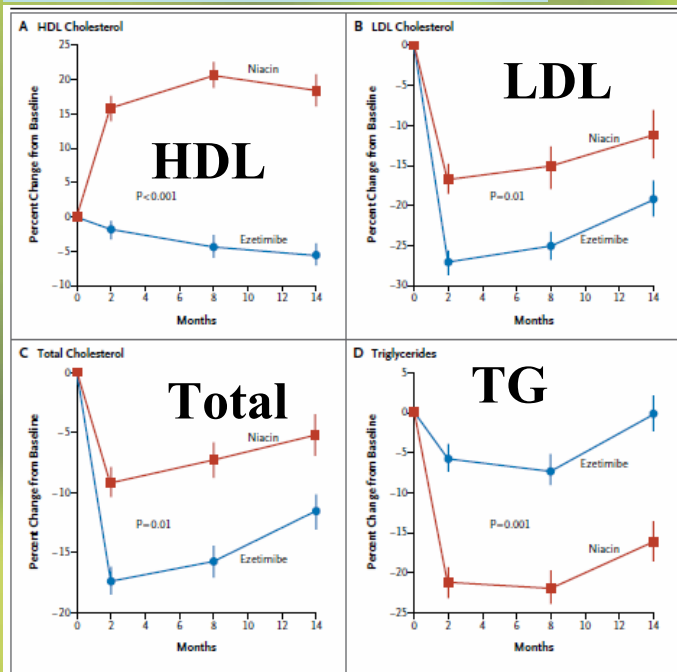


Figure 1. Mean Percent Changes in Cholesterol and Triglyceride Levels over the 14-Month Study Period among the 208 Patients Who Completed the Study, According to Treatment Group. P values are given for the comparison between the two treatment groups at 14 months. The vertical bars indicate the standard errors. HDL denotes high-density lipoprotein, and LDL low-density lipoprotein.

Niacin more effective at reducing the plaque?

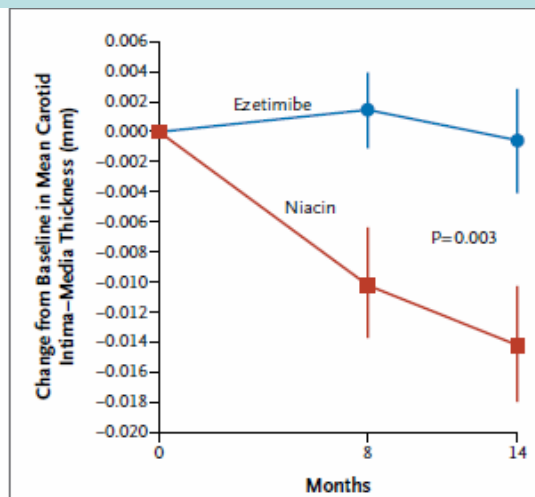


Figure 2. Changes in the Mean Carotid Intima–Media Thickness over the 14-Month Study Period, According to Treatment Group.

The carotid intima–media thickness is the thickness of the far wall of the bilateral distal common carotid arteries, measured in millimeters. The P value is given for the comparison of repeated measures of the carotid intima–media thickness over the 14-month period. The vertical bars indicate the standard errors.



Conclusion ?

- **The target of $\geq 50\%$ LDL is acceptable in most**
- **2 mmol/L target – more info to come?**



UNIVERSITY OF
SASKATCHEWAN

