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2005 춘계 순환기 통합학술대회
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Do We Have All Answers with Statins In Treating Patients with Hyperlipidemia?

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Papers Related to Hyperlipidemia by *Koh KK* et al

- *Circulation* 1999;99:354-360
- *Circulation* 2001;103:1961-1966
- *Circulation* 2002;105:1531-1533
- *Arterioscler Thromb Vasc Biol* 2002;22:e19-e23
- *Circulation* 2004;110:3687-3692
- *J Am Coll Cardiol* 2005 (May, in press)
- *Diabetes Care* 2005 (June, in press)

Are you satisfied with Statins?

NO? Why?

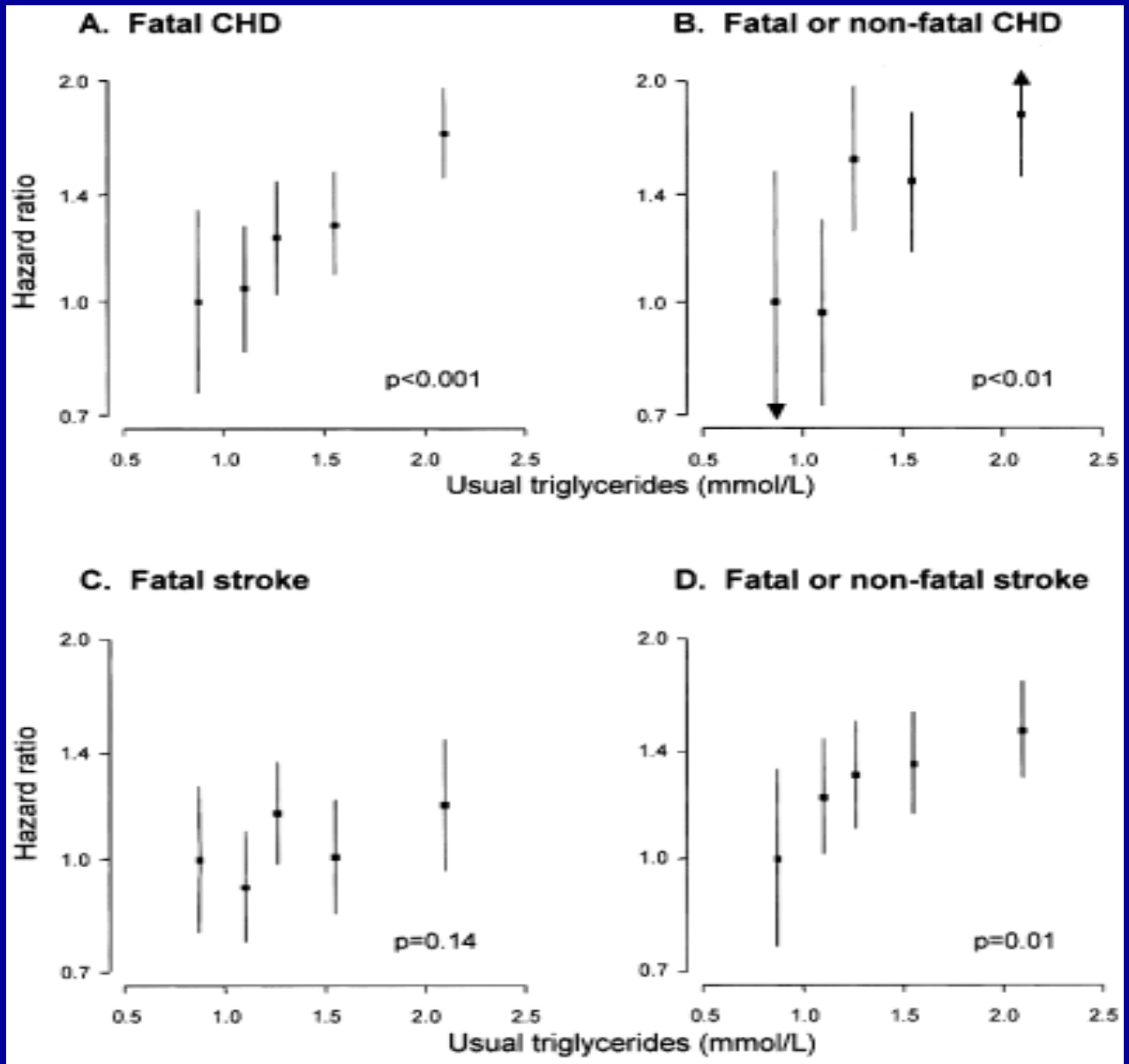
- Many statin-treated patients still have an initial or recurrent CHD event, despite reductions in LDL cholesterol.

Sacks FM, et al. Circulation 2000;102:1893

HPS study. Lancet. 2002;360:7

- TG increase and HDL-C less increase

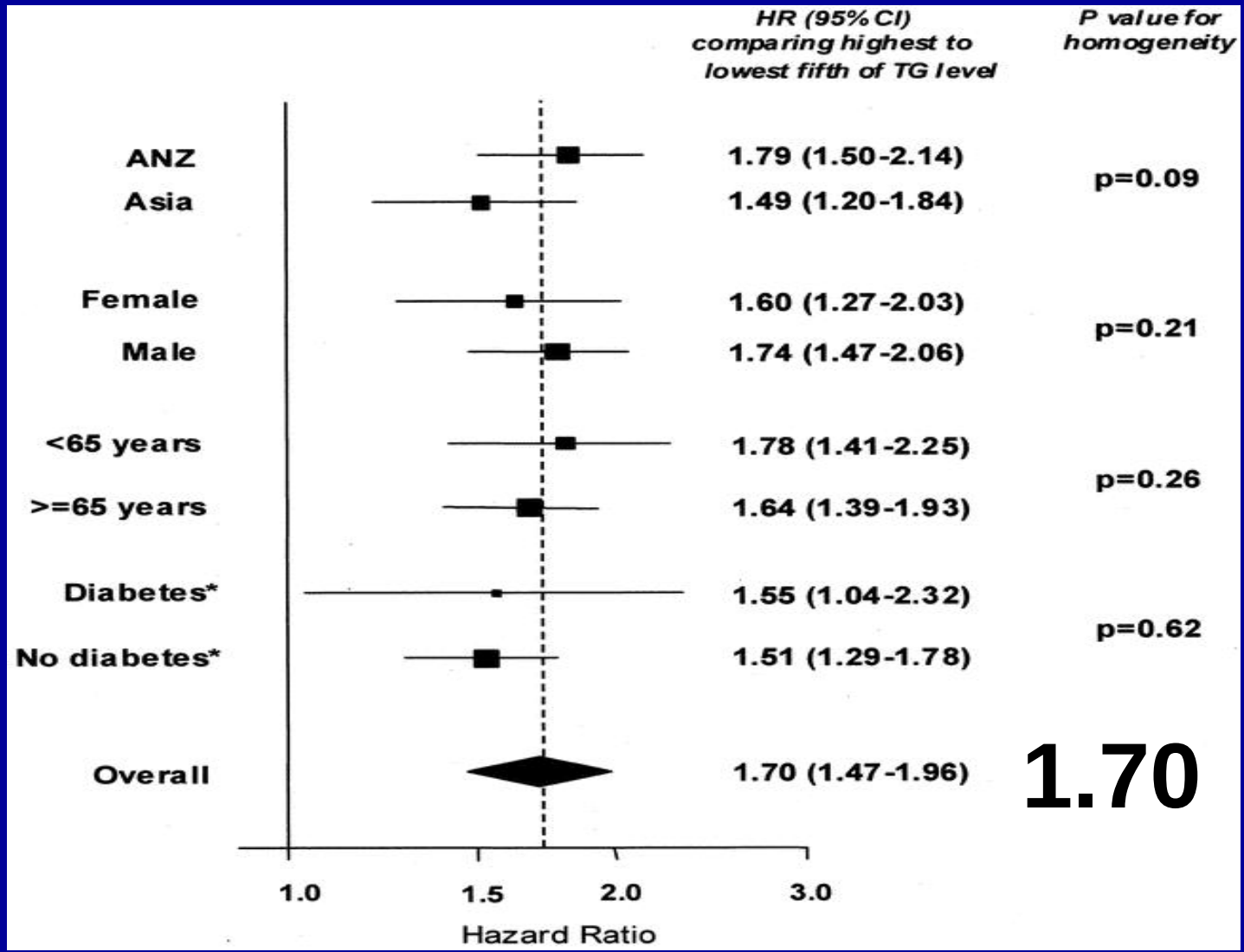
Serum TG as Risk Factor for CVD In the Asia-Pacific Region



Meta-analysis of 26 prospective studies 96,224 individuals

Circulation 2004;110:2678

Hazard Ratios comparing within subgroups Risk of fatal CHD between individuals belonging To highest vs. lowest fifth of TG levels



NCEP ATP III (2001)

- **High TG, >200 mg/dl and Low HDL-C, <40 mg/dl: Risk Factor**
- **Insulin resistance syndrome and Metabolic Syndrome**
- **Diabetes: CHD equivalent**

NCEP, Adult Treatment Panel III. JAMA. 2001

Metabolic Effects of Statins

- Simvastatin either did not change or worsened insulin sensitivity in diabetic patients

  Farrer M, Diabetes Res Clin Pract. 1994;23:111
  Ohrvall M, Metabolism. 1995;44:212

- Statins particularly high dose may increase the onset of new diabetes. **Atorvastatin 80 mg** was associated with a statistically significant increased risk of developing a HbA_{1c}>6 both in non-diabetics (adjusted HR 1.78) and in diabetics (adjusted HR 2.36). The pooled adjusted HR was **1.84** (p<0.0001).

  A PROVE-IT TIMI 22 Substudy
  Circulation. 2004;110:III-834

High-sensitivity CRP levels are Important

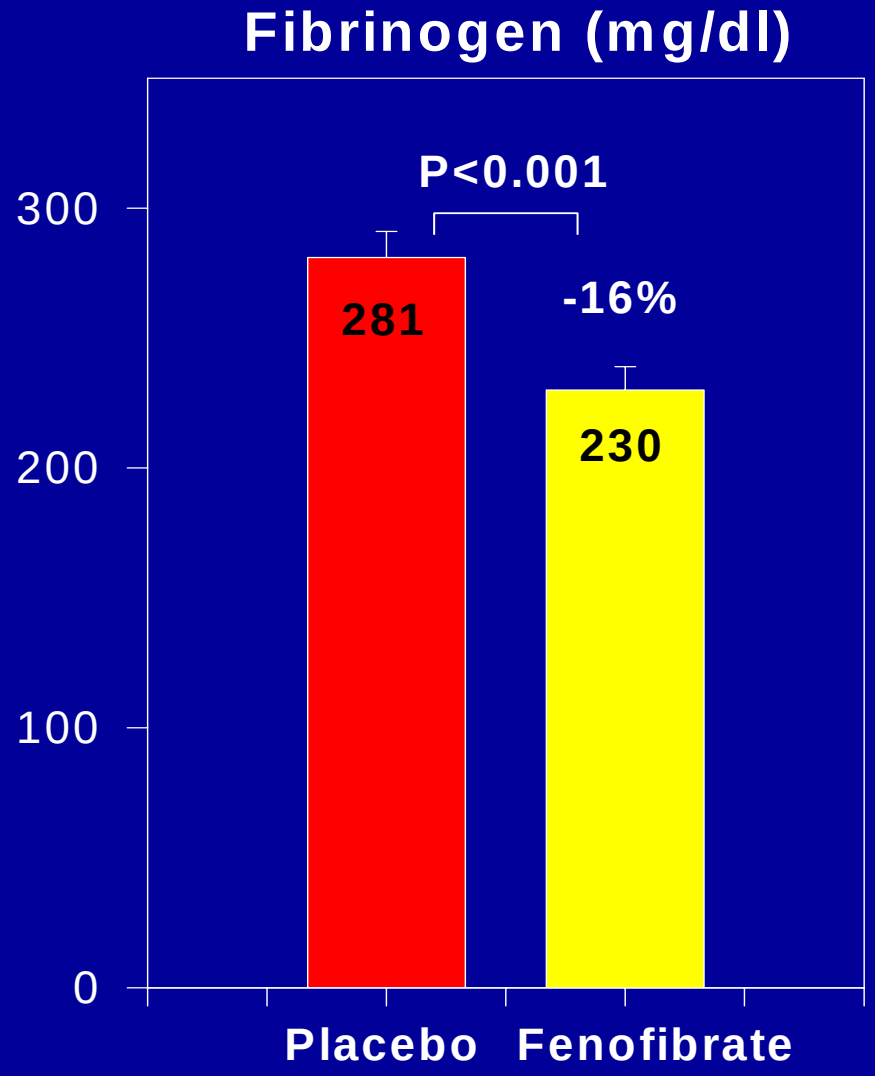
- After statin therapy, the reduced progression of atherosclerosis is significantly related to greater reductions in CRP levels.

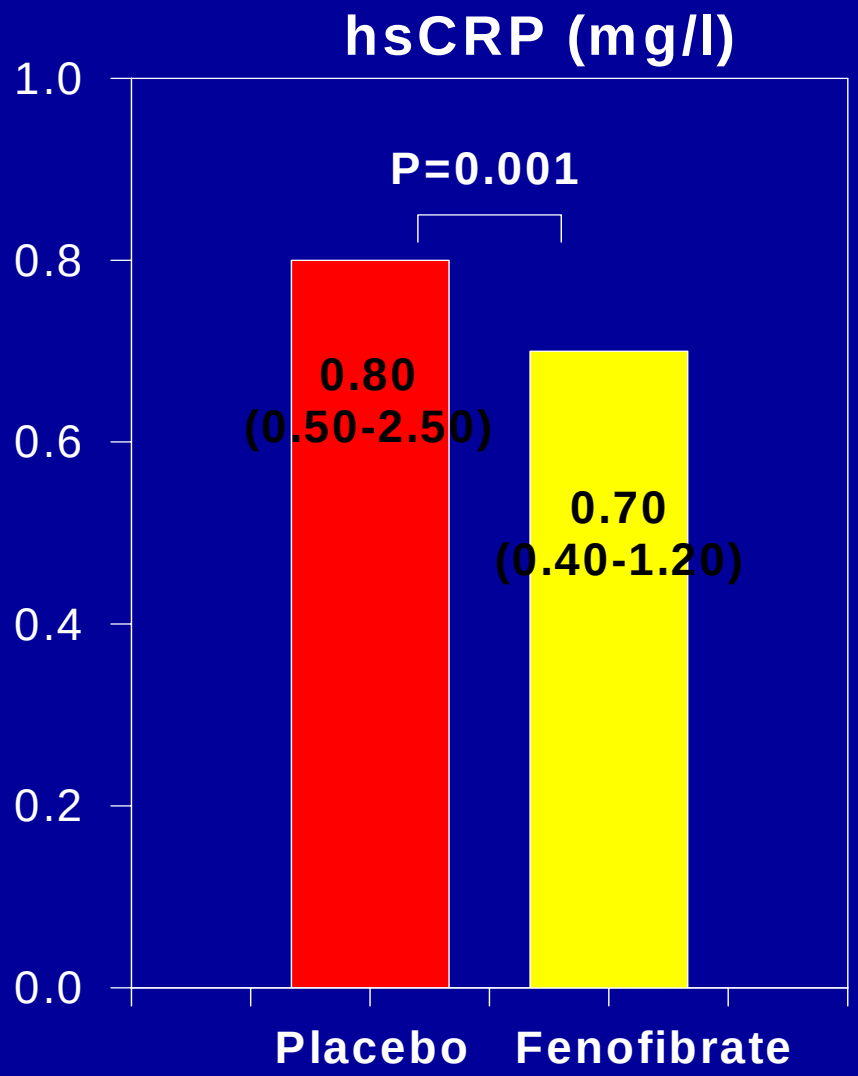
Nissen SE, et al. N Engl J Med. 2005;352:29.

- Patients with **low CRP levels** have better clinical outcomes than those with higher CRP levels, **regardless of LDL cholesterol level**.

Ridker PM, et al. N Engl J Med. 2005;352:20.

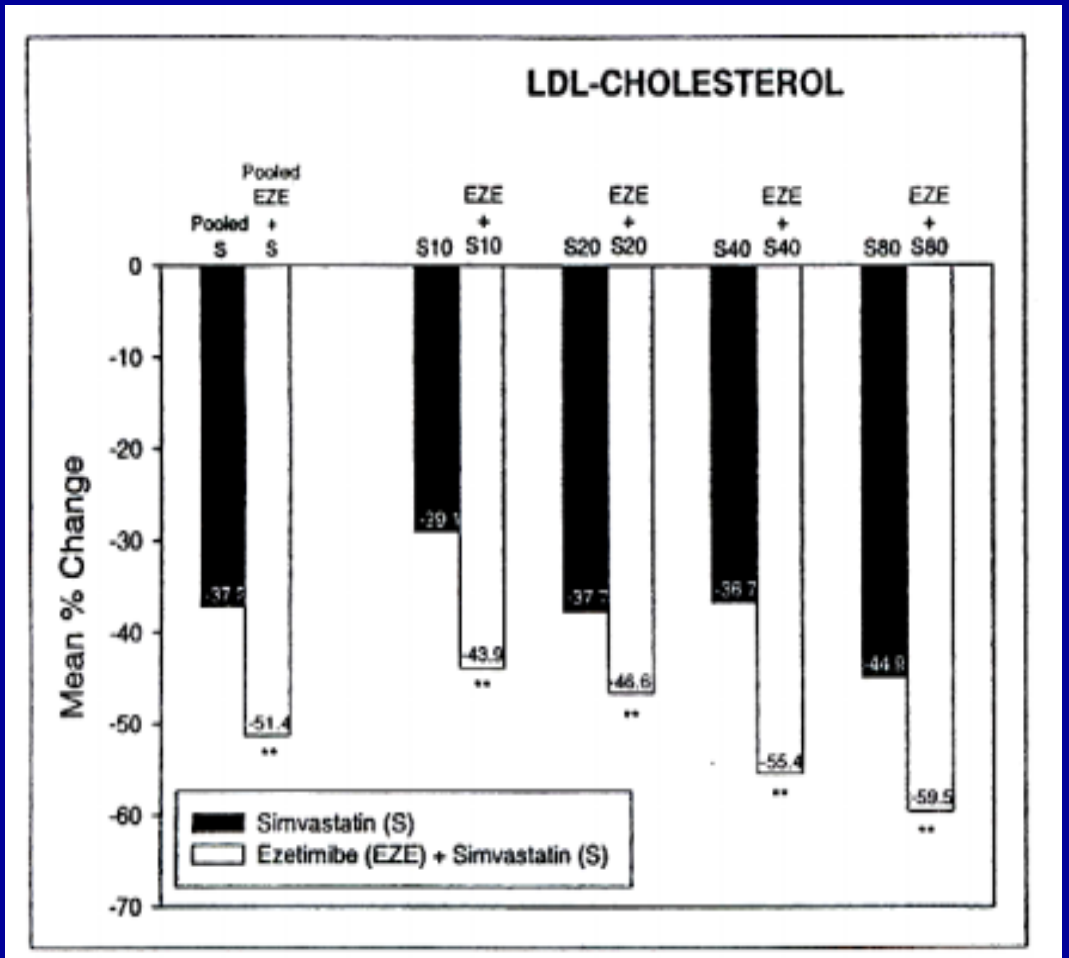
Effects of Fenofibrate on Acute Phase Reactants In 46 Hypertriglyceridemic Patients

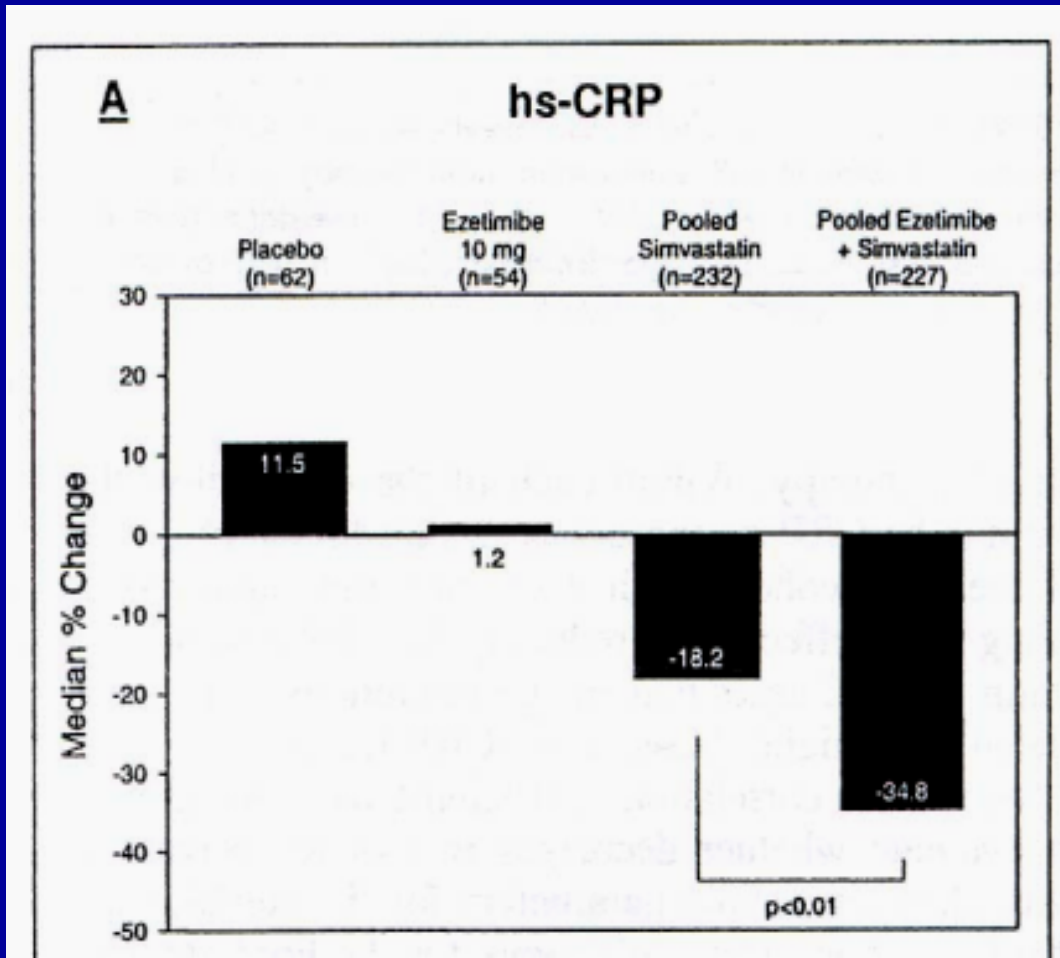




Koh KK, et al. Diabetes Care;2005:June

Effect of Coadministration of Ezetimibe And Simvastatin on hs-CRP





Sager PT, et al. Am J Cardiol. 2003;92:1414.

Beneficial Vascular and Metabolic Effects of Combined Therapy with *Ramipril* and Simvastatin in 50 Patients with Type 2 Diabetes

Kwang Kon Koh, Seung Hwan Han

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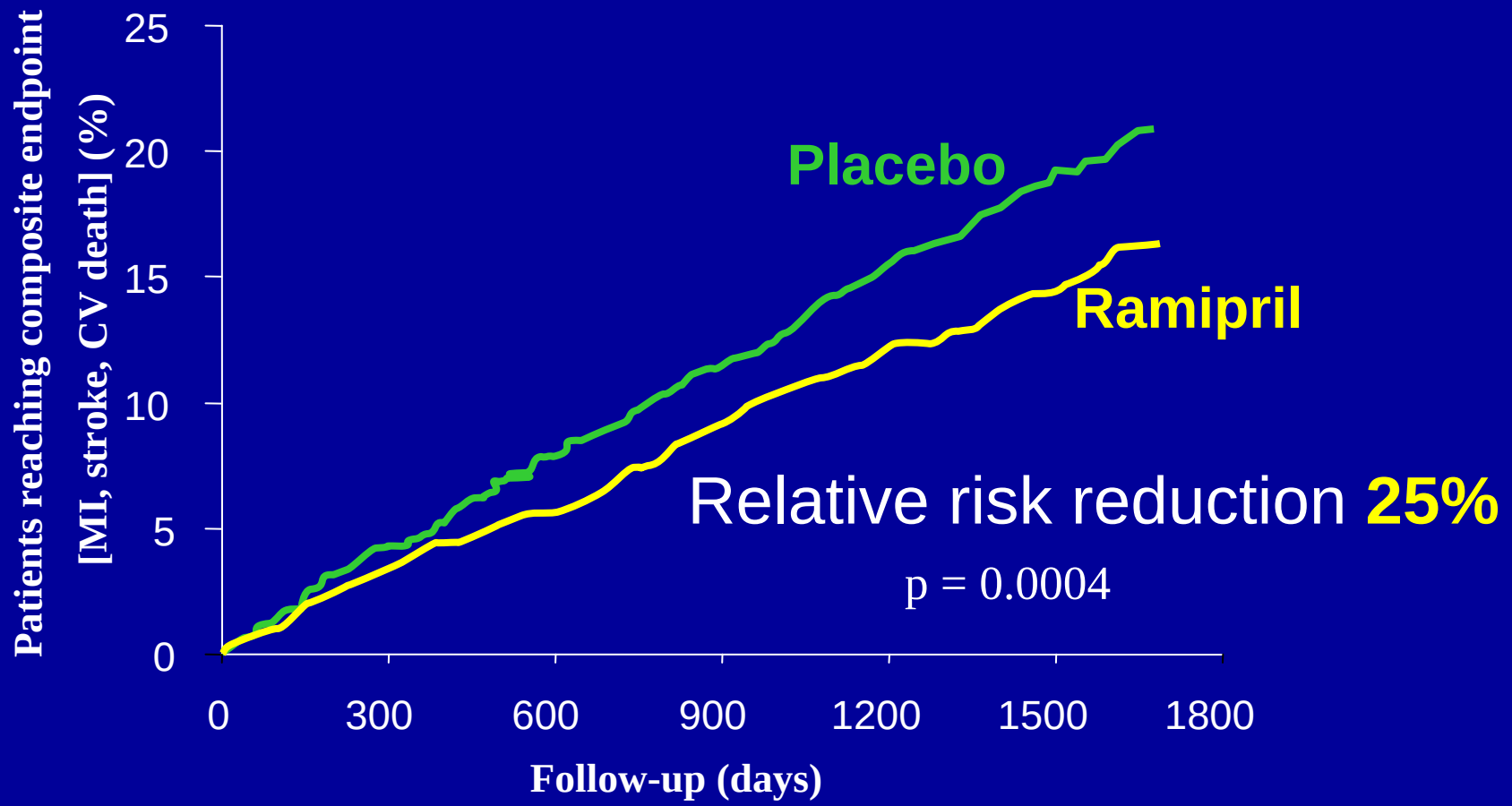
Incheon, Korea
Diabetes Unit, NIH, USA*

AHA 2004, Hypertension 2005 (June)

MICRO-HOPE : CV outcomes



The Lancet, 2000; 355: 253

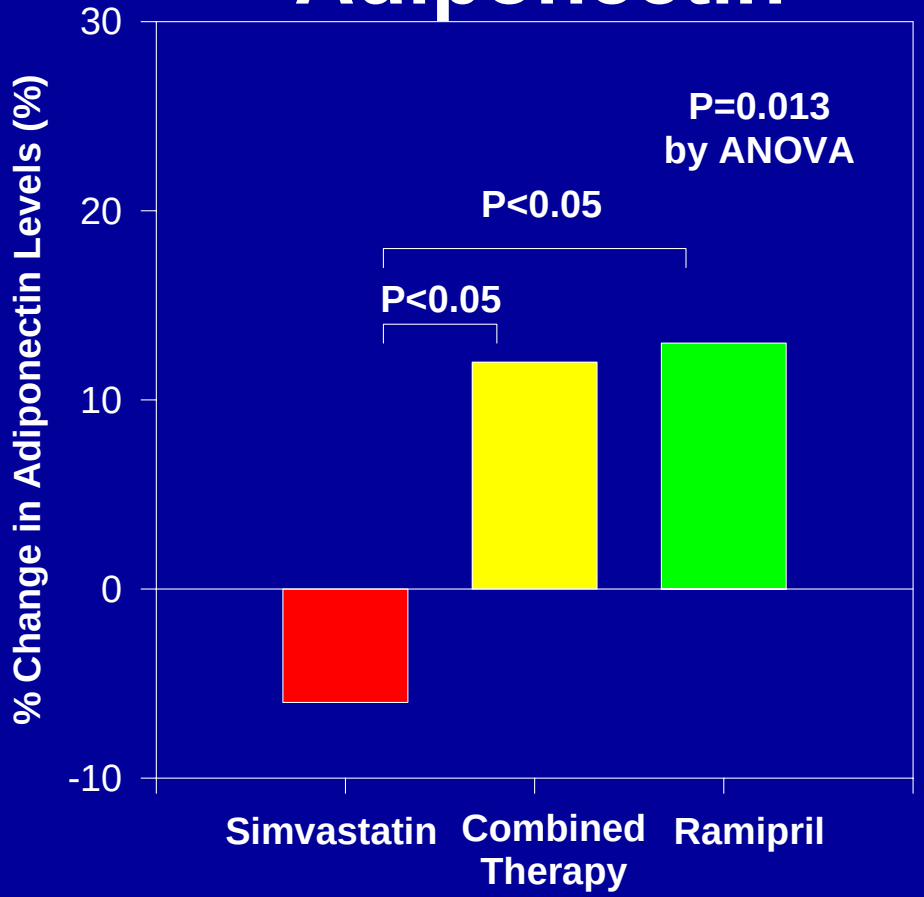
Additive Effect on top of all other Medications

Concomitant Medications

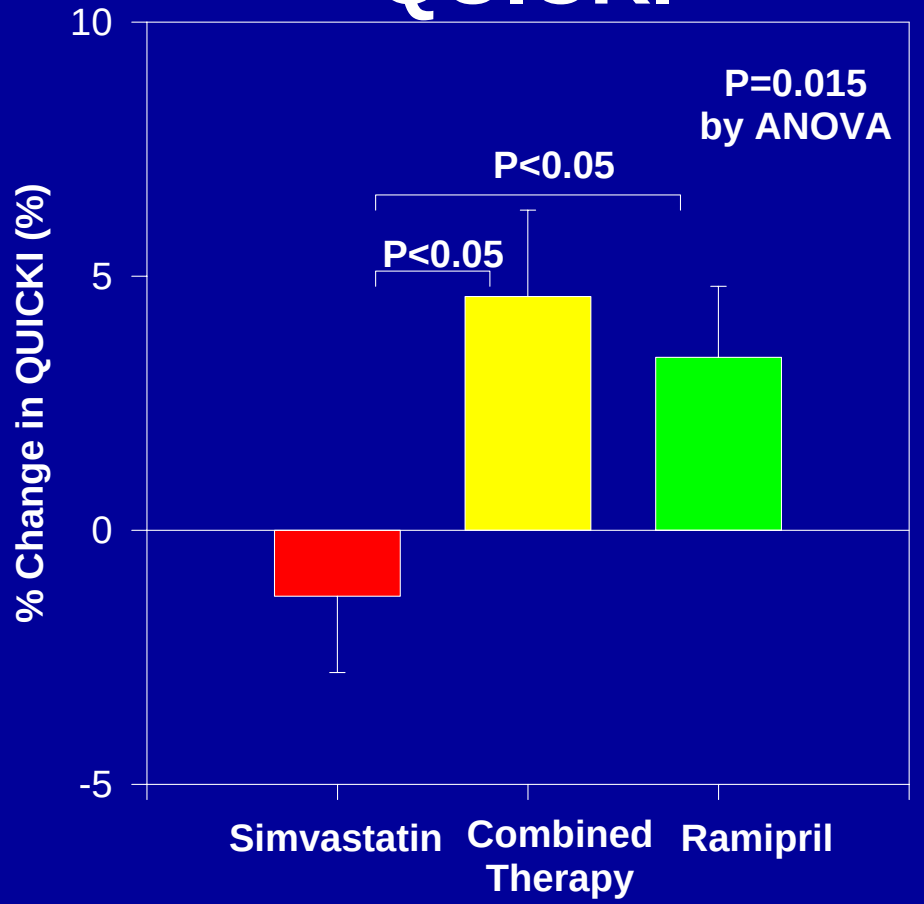
▪ Dietary alone	18%	Aspirin	54 %
▪ Oral agents	53%	Lipid lowering agents	23 %
▪ Insulin	24%	CCB	43%
▪ Insulin+oral agents	5%	Others: Beta-blockers	28 %
		Diuretics	19 %

Effects of Simvastatin, Combined Therapy, and Ramipril on Insulin Sensitivity

Adiponectin



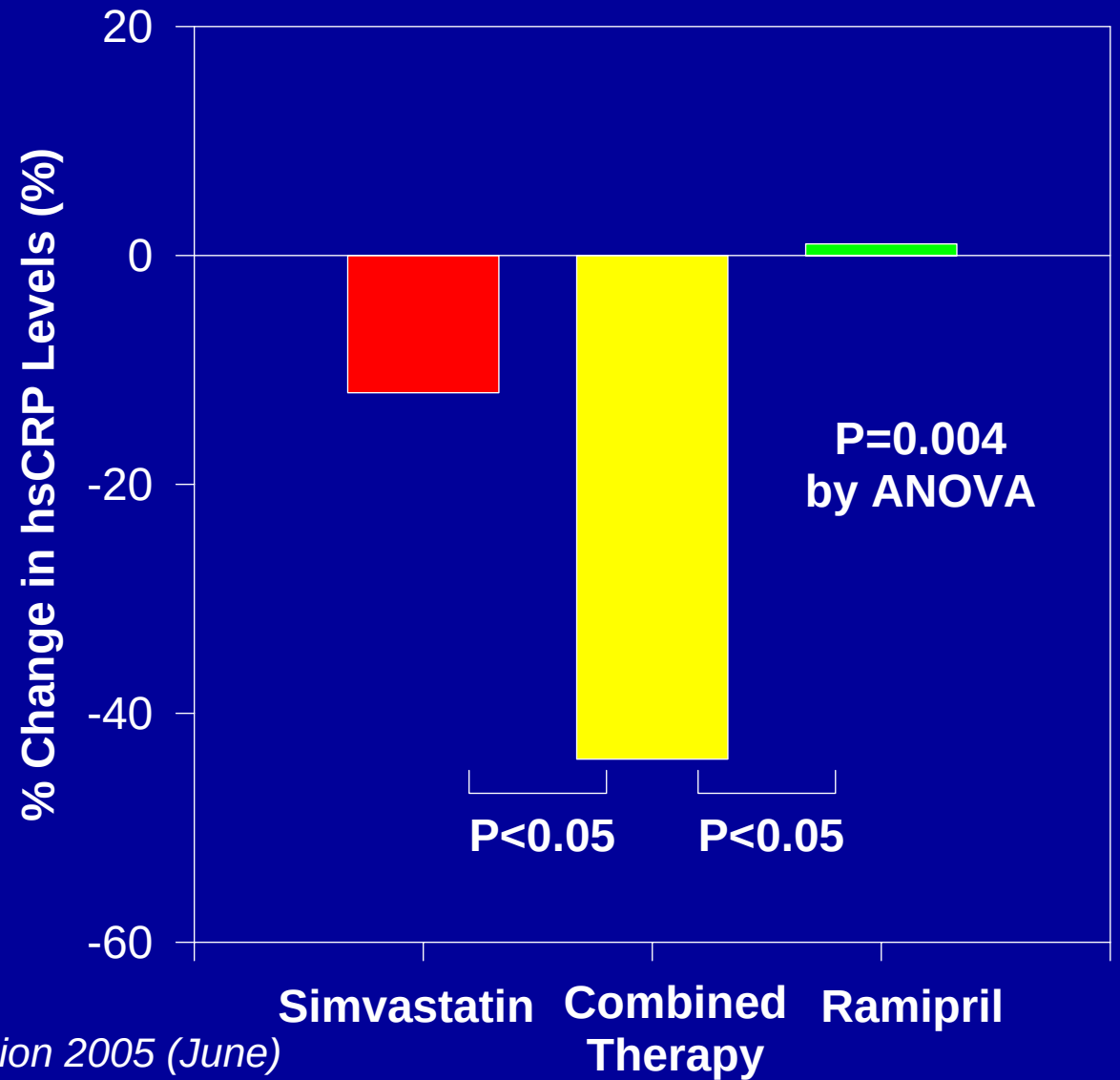
QUICKI



*QUICKI=Quantitative Insulin-Sensitivity Check Index, a surrogate index of insulin sensitivity, QUICKI = 1/[log(insulin)+log(glucose)]

Koh KK, et al. Hypertension 2005 (June)

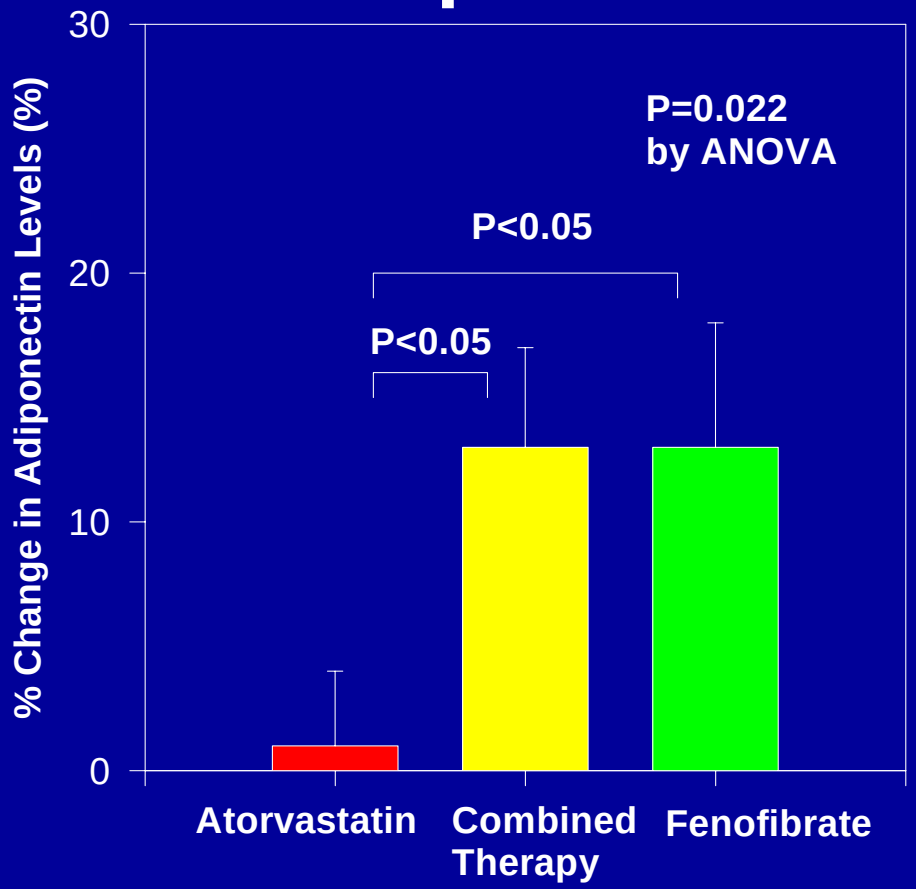
Effects of Simvastatin, Combined Therapy, and Ramipril on hsCRP Levels



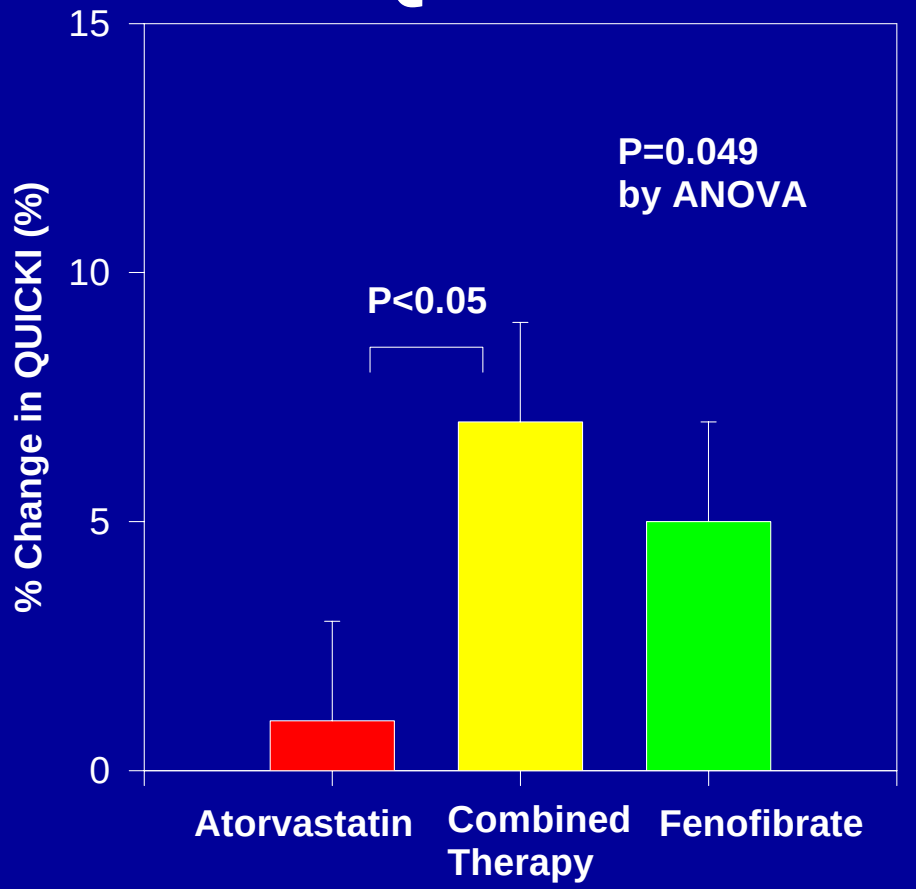
Koh KK, et al. Hypertension 2005 (June)

Effects of Atorvastatin, Combined Therapy, and Fenofibrate on Insulin Sensitivity

Adiponectin



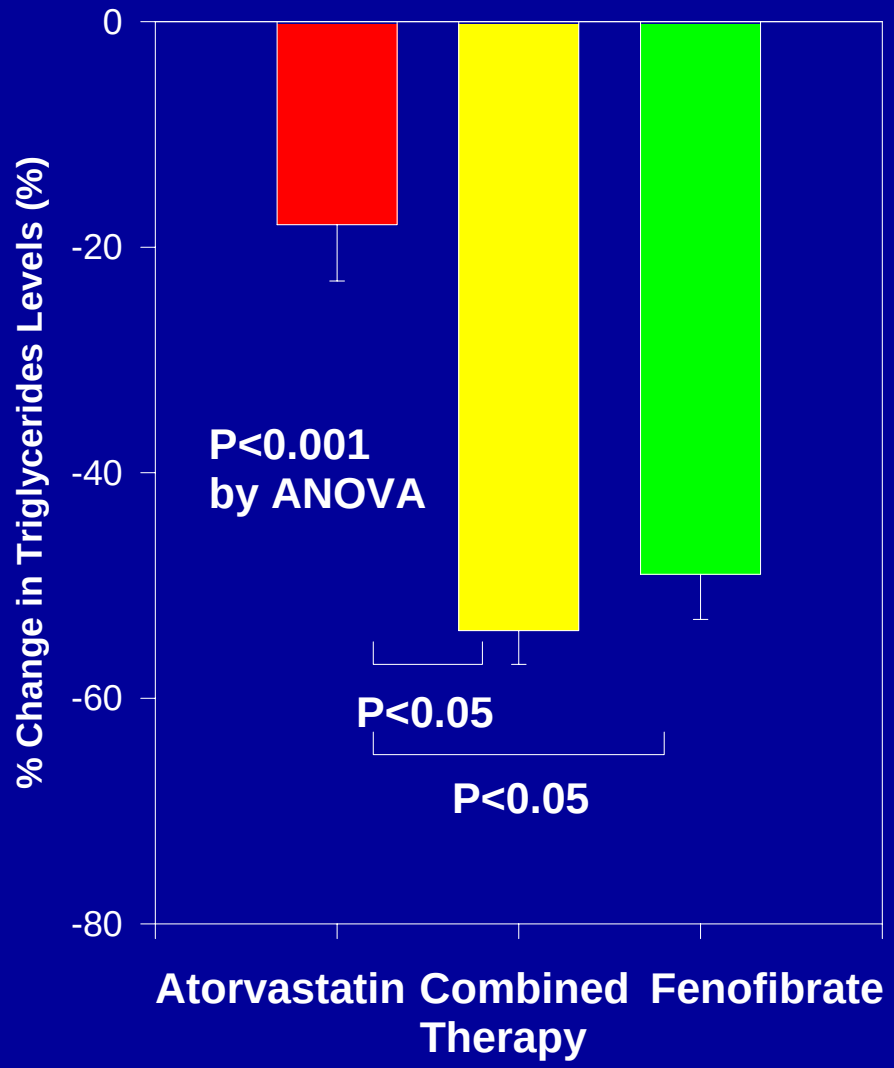
QUICKI

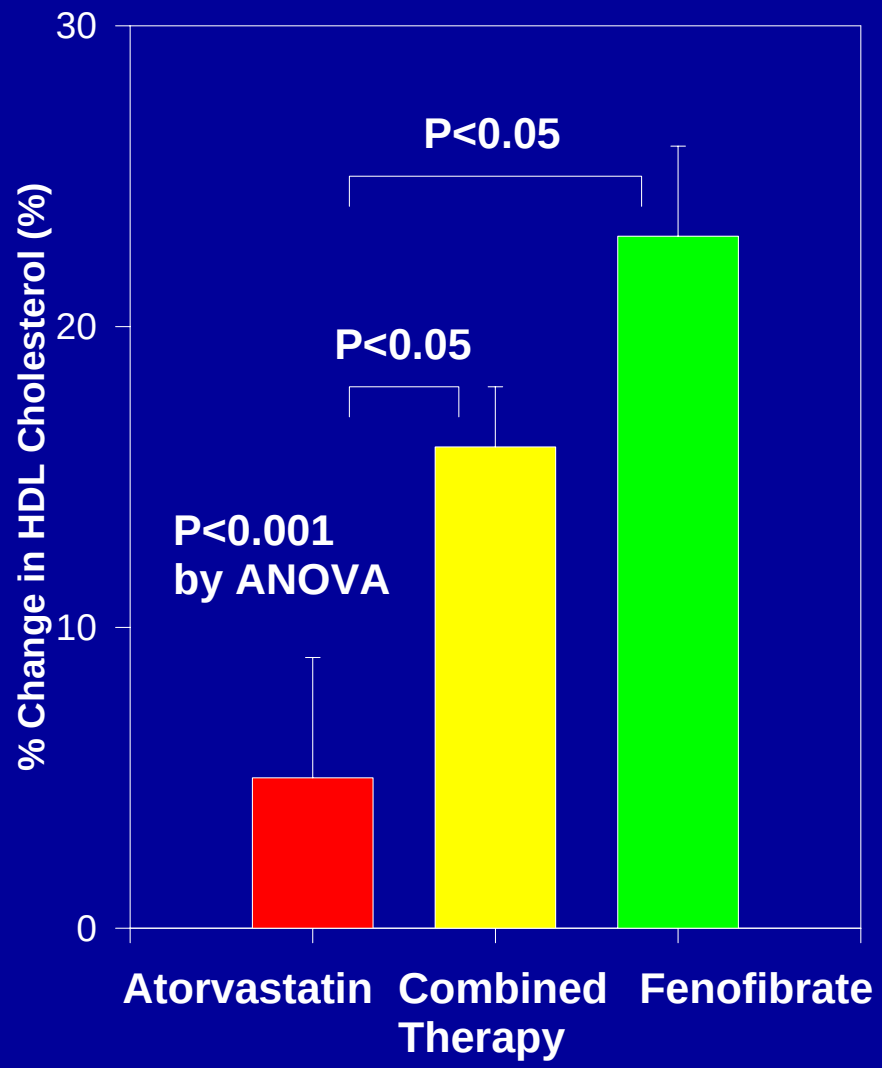


*QUICKI=Quantitative Insulin-Sensitivity Check Index, a surrogate index of insulin sensitivity, QUICKI = 1/[log(insulin)+log(glucose)]

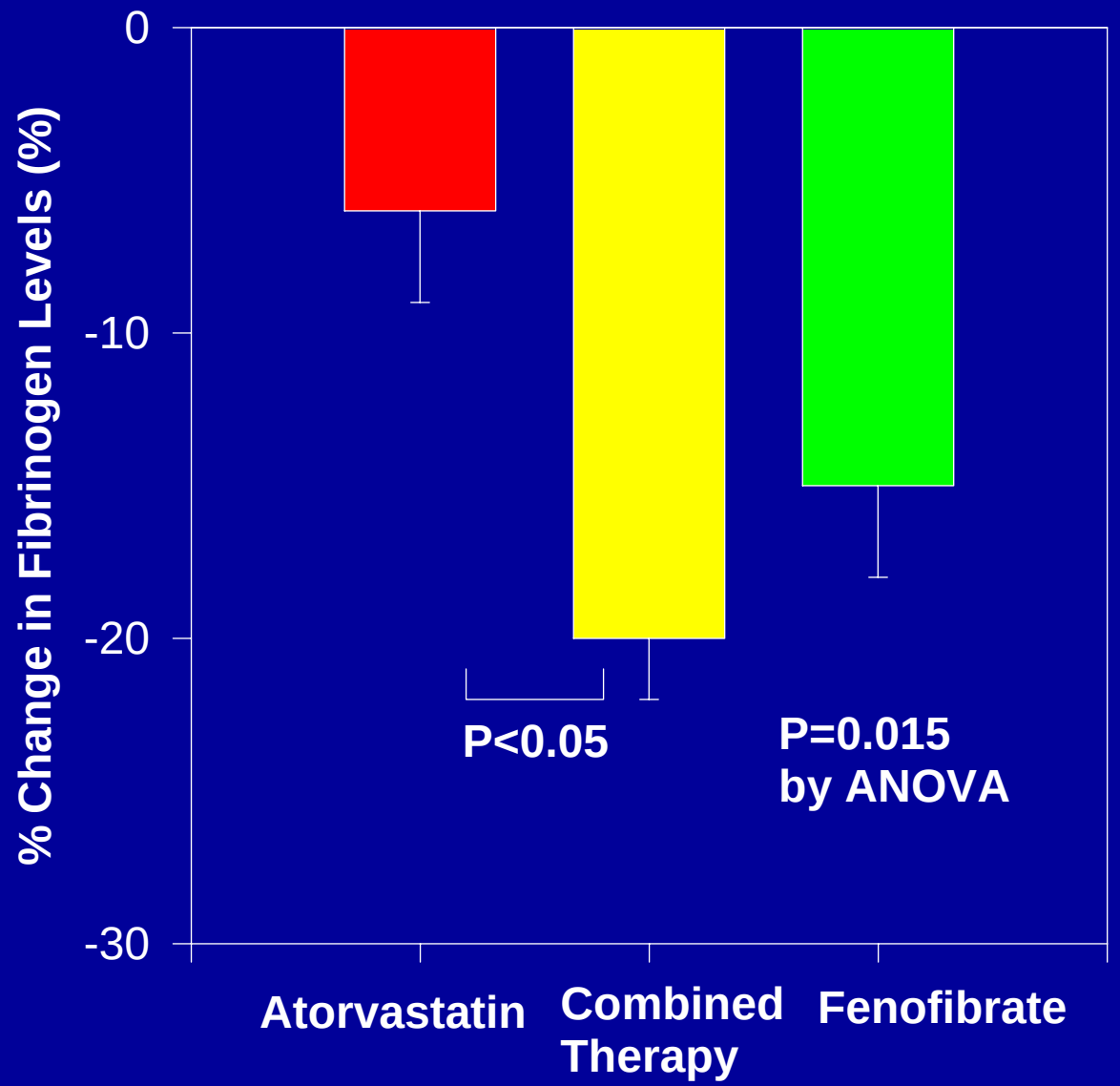
Koh KK, et al.
JACC 2005 (May)

Combined Therapy or Fenofibrate Alone Significantly Changes TG and HDL-C Levels





Combined Therapy or Fenofibrate Alone Significantly Lowers Fibrinogen Levels

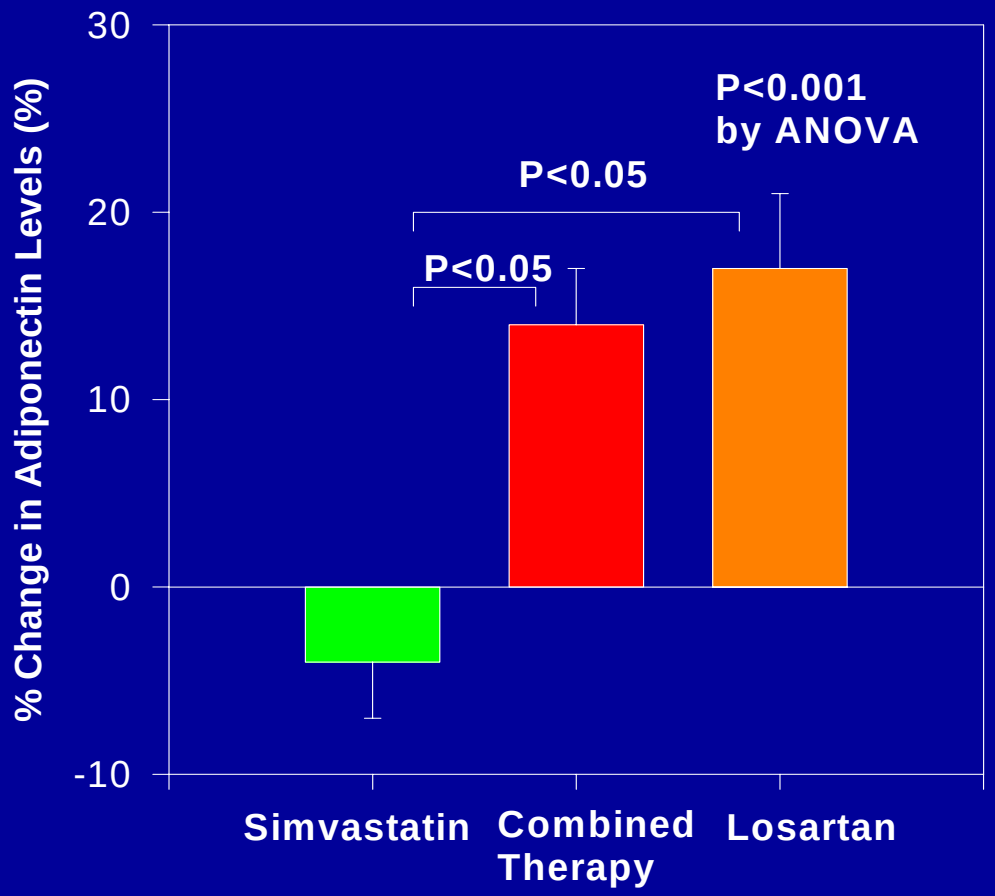


Koh KK, et al.

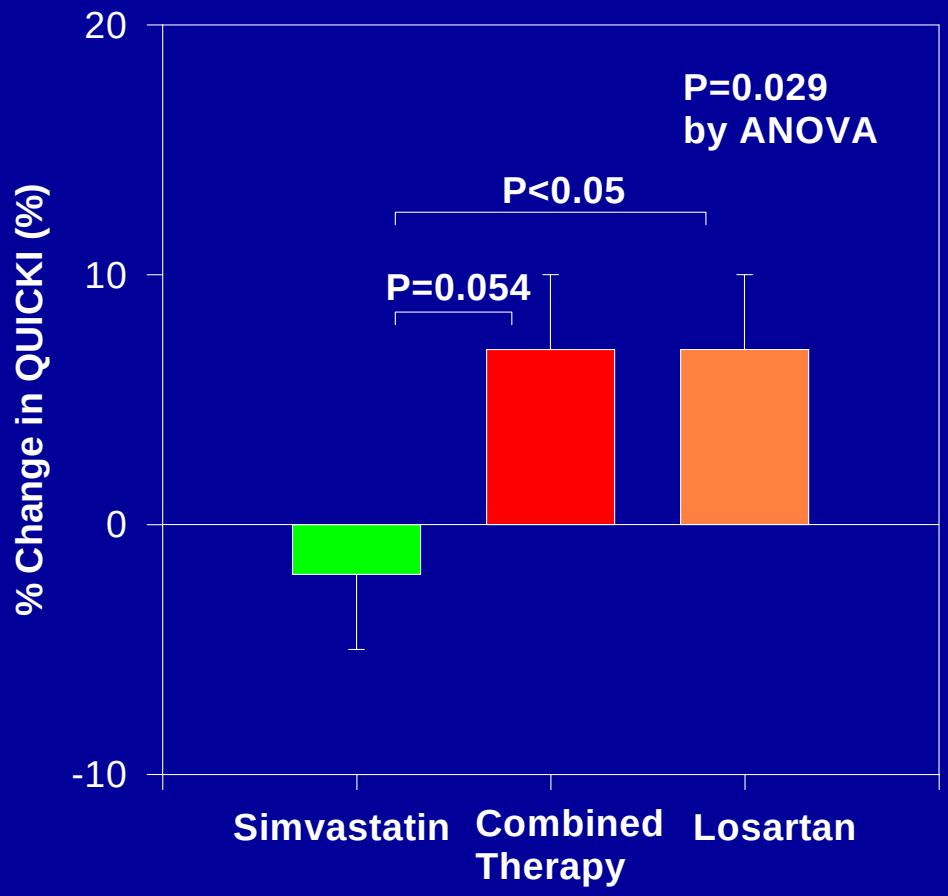
JACC 2005 (May)

Effects of Simvastatin, Combined Therapy, and Losartan on Insulin Sensitivity

Adiponectin

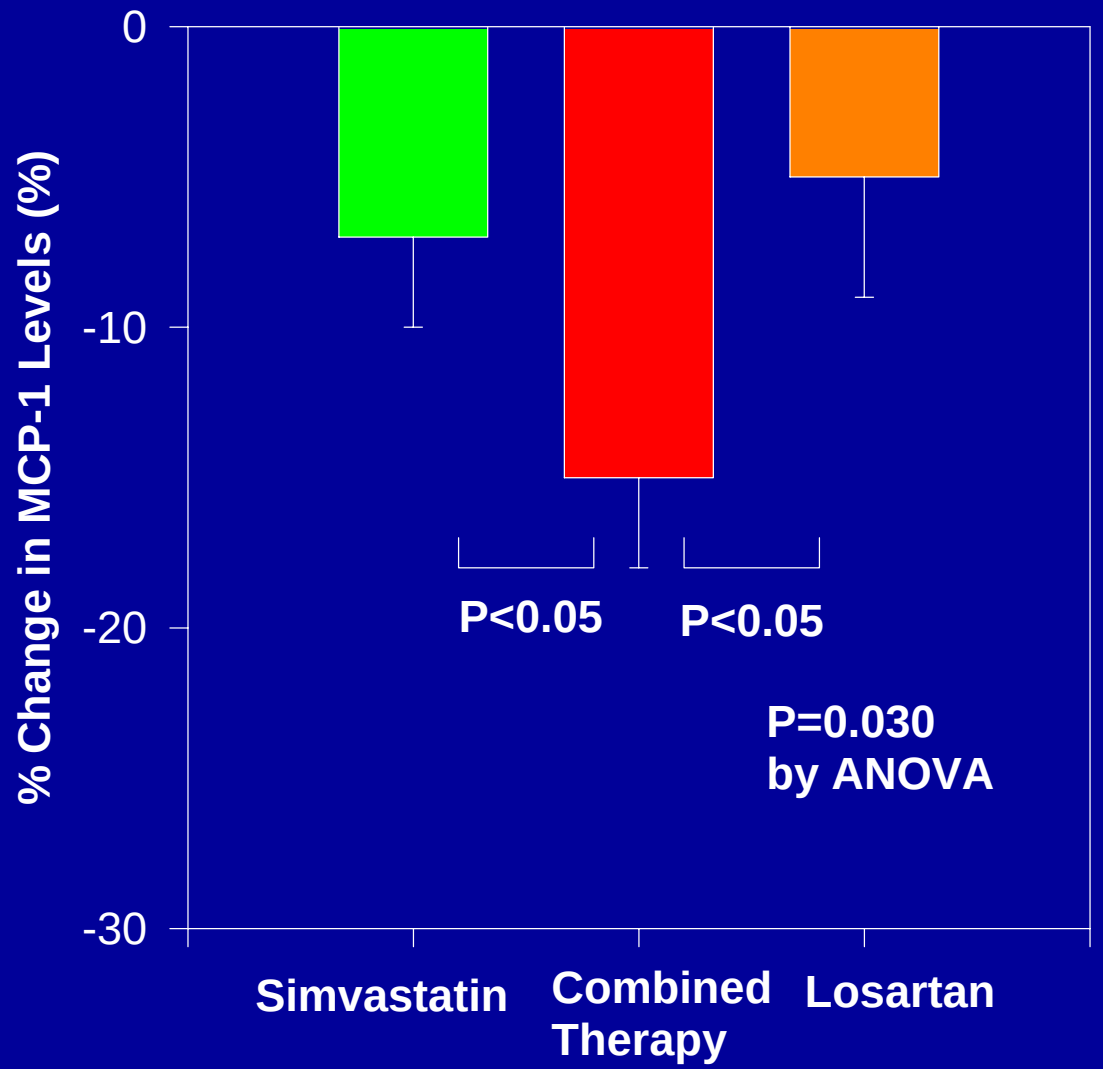


QUICKI



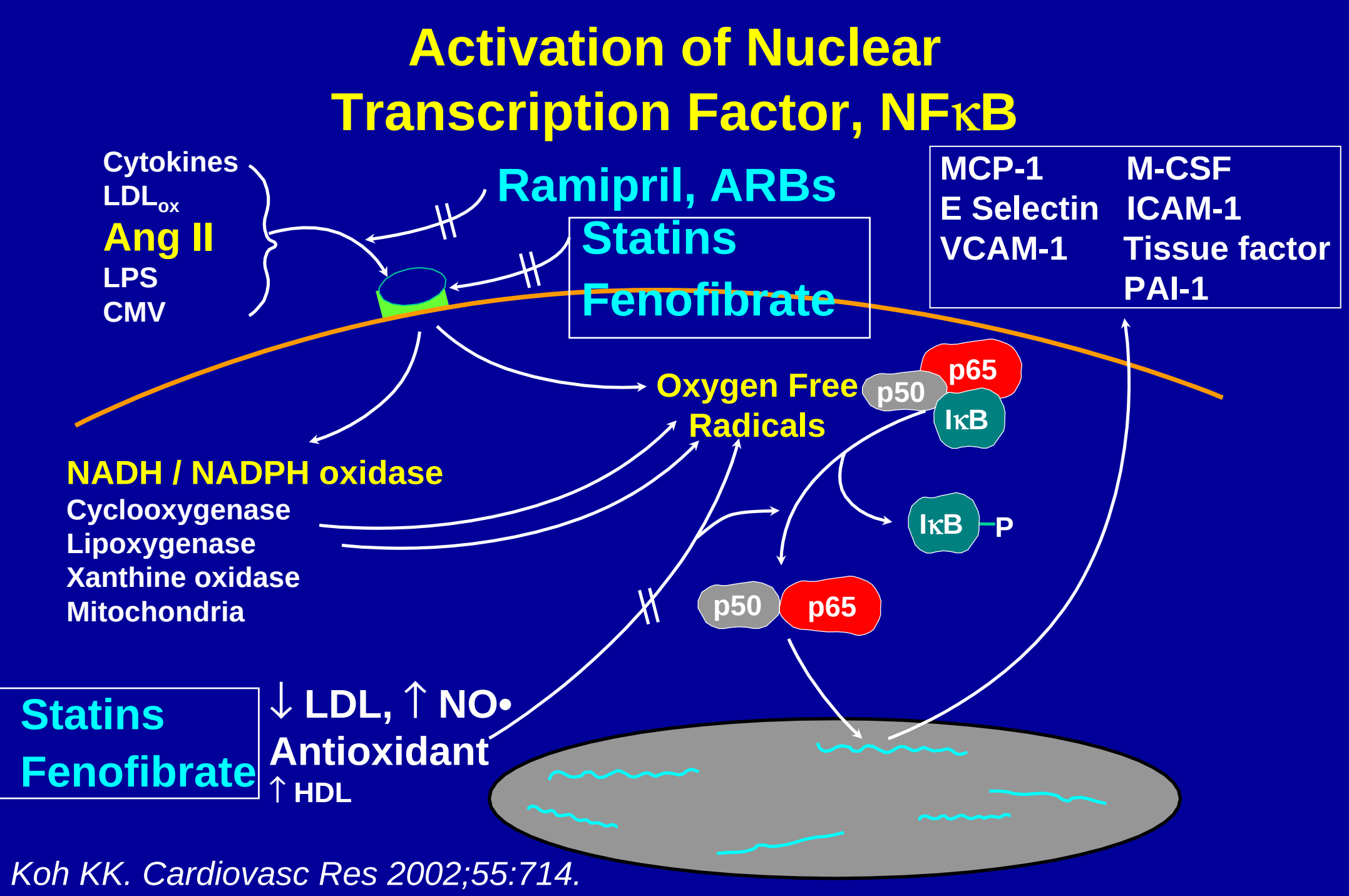
Koh KK, et al. Circulation 2004;110:3687

Combined Therapy Significantly Reduces MCP-1 Levels



Koh KK, et al. Circulation 2004;110:3687

Activation of Nuclear Transcription Factor, NFκB



Koh KK. Cardiovasc Res 2002;55:714.

Why Is PEACE Trial Neutral?

1. Underpowered trial- only 8290 of a planned 14,100 patients were enrolled
2. Primary outcome was changed to include revascularization
3. Failure to reach maximal dose because of adverse effects

Meta-analysis of the HOPE, PEACE, and EUROPA data shows significant reductions in mortality, reinfarction, and stroke

Yusuf S, Pogue J. N Engl J Med 2005;352:937
Myers MG. N Engl J Med 2005;352:938

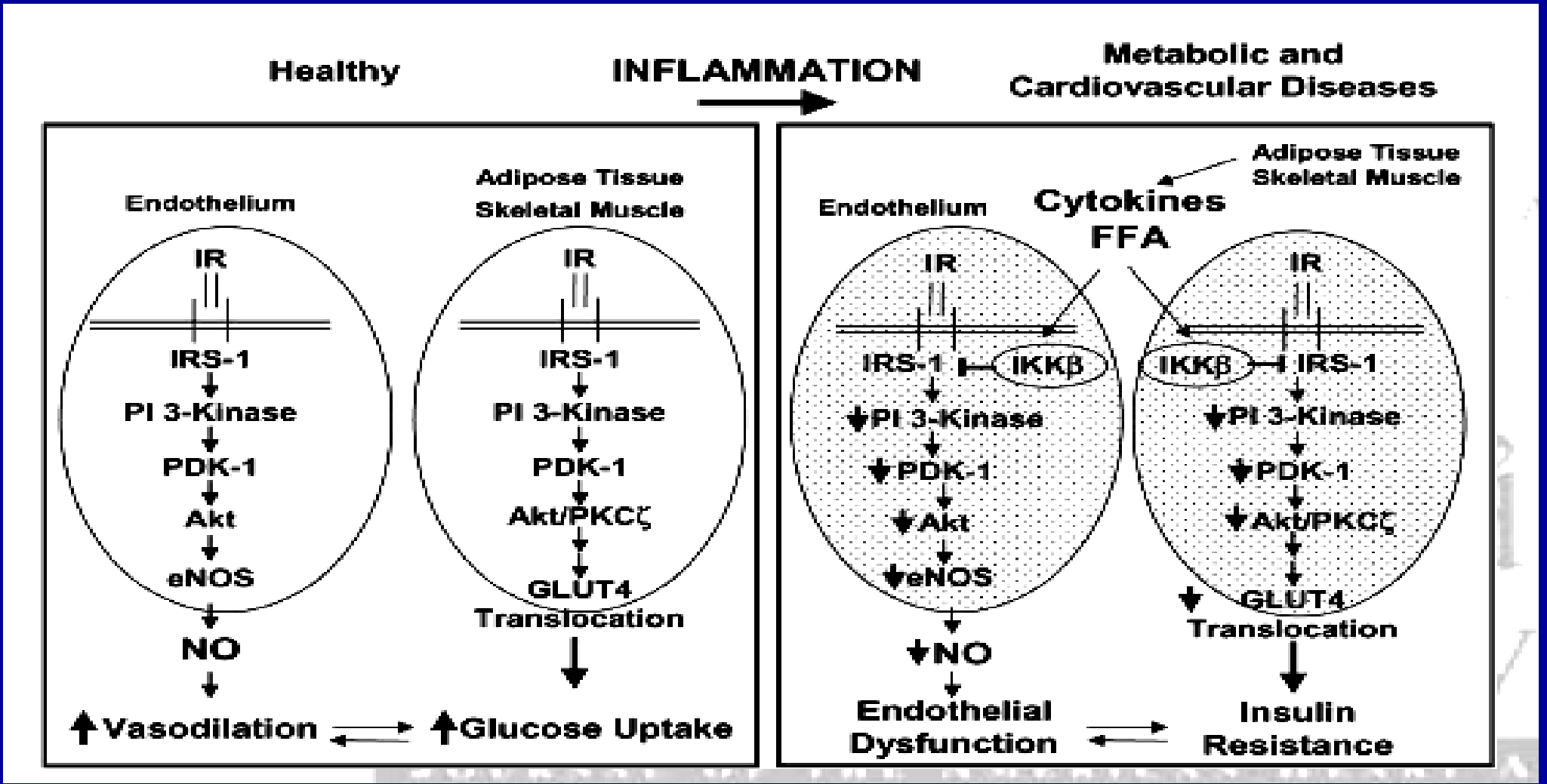
Meta-analysis of Data on Mortality from HOPE, EUROPA, and PEACE Trials

Trial	ACEI	Control	OR	P value
HOPE	10.4%	12.2%	0.83 (0.73-0.95)	0.005
EUROPA	6.1%	6.9%	0.89 (0.77-1.02)	0.098
PEACE	7.2%	8.1%	0.88 (0.75-1.04)	0.126
Total	**7.8%**	**8.9%**	**0.86 (0.79-0.94)**	**<0.001**

Meta-analysis shows significant reductions in mortality, reinfarction, and stroke

Yusuf S, Pogue J. N Engl J Med 2005;352:937

Cross-talk between inflammatory and insulin signaling pathways causes both endo. dysfunction and metabolic insulin resistance that synergize to cardiovascular disorders in Met Syndrome



Kim J, Koh KK, Quon MJ. Arterioscler Thromb Vasc Biol 2005 (Editorial, May)

결론

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Acknowledgment

- **Seung Hwan Han, MD**
- **Eak Kyun Shin, MD**
  Cardiology

- **Jeong Yeal Ahn, MD**
  Laboratory Medicine

- Michael J. Quon**, MD**, PhD
  Diabetes Unit, NIH, USA

시간지키기