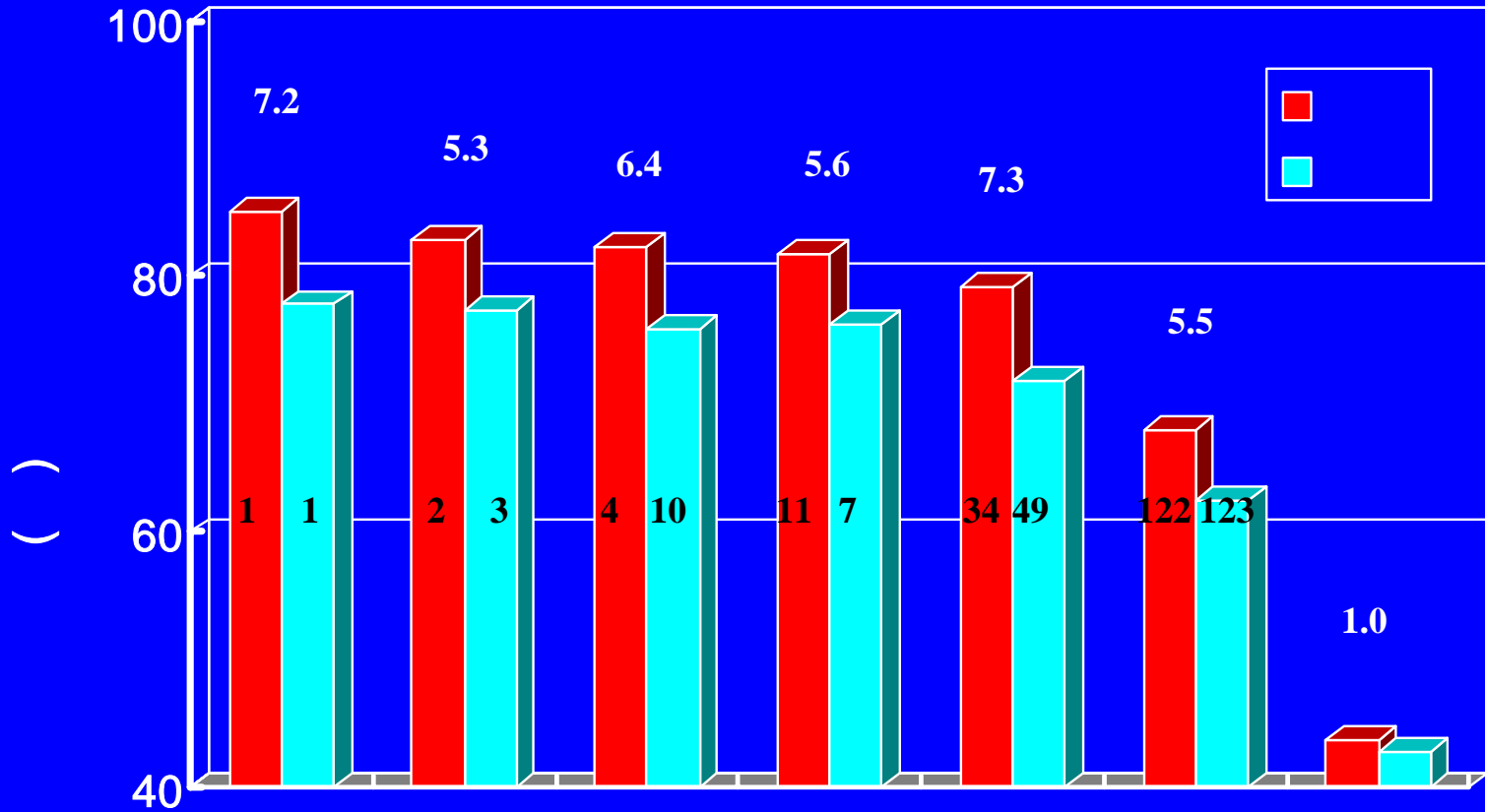


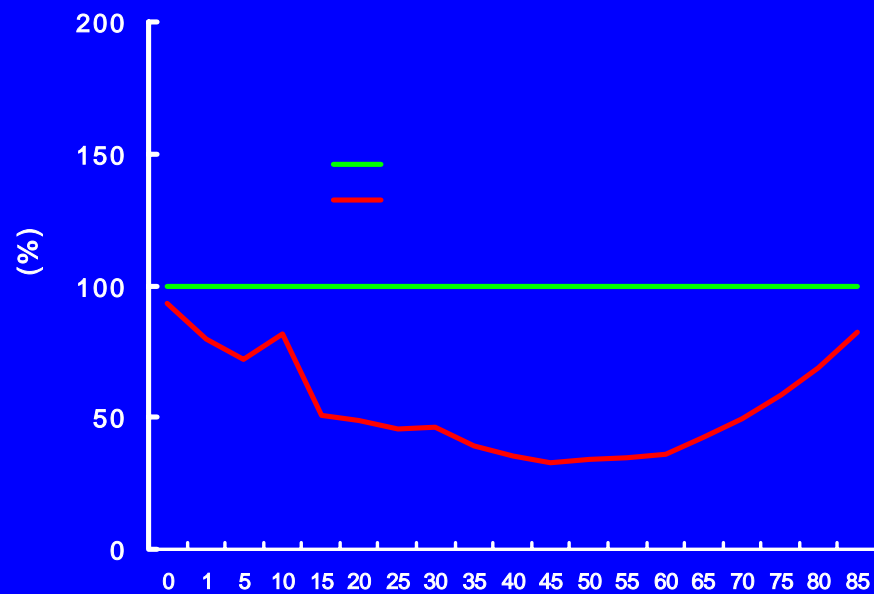
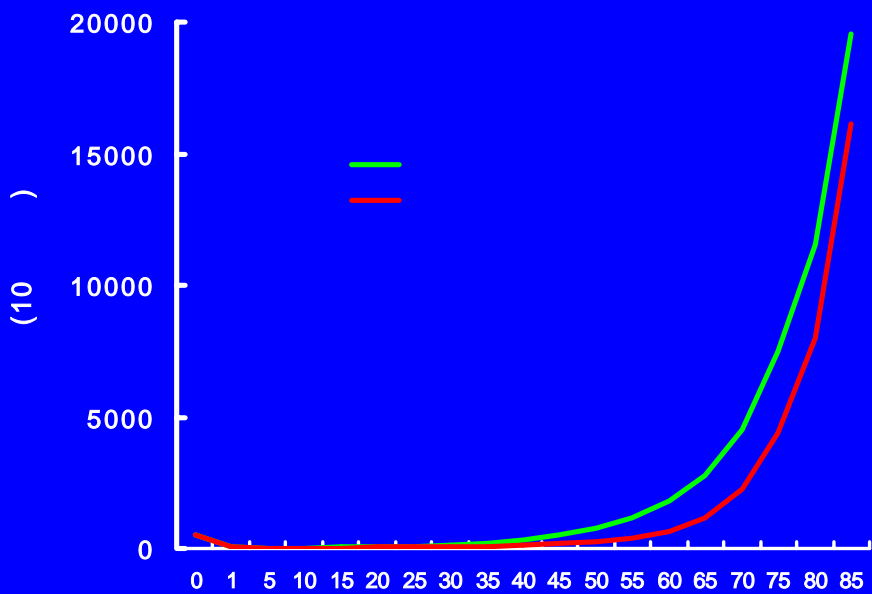
Treatment and Role of Hormone Replacement Therapy

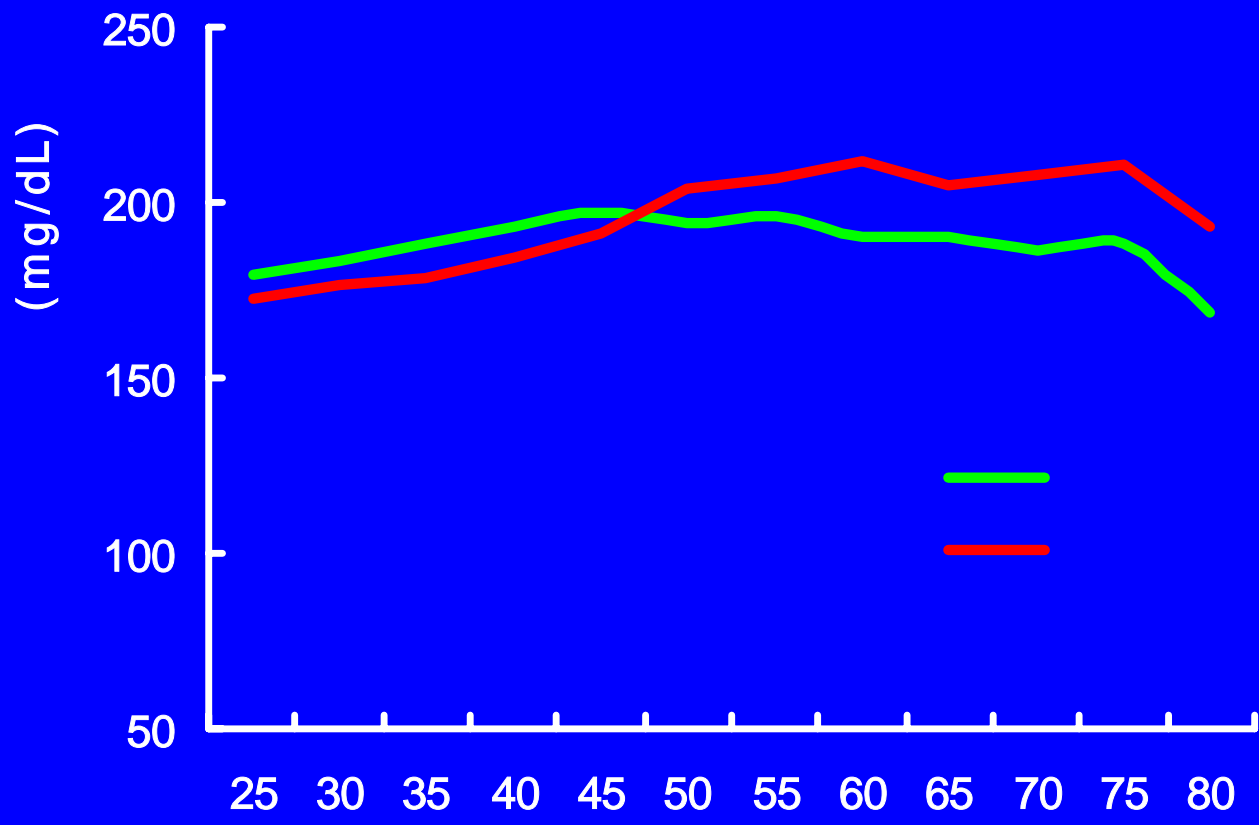
Chung-Ang University Hospital
Chee Jeong Kim

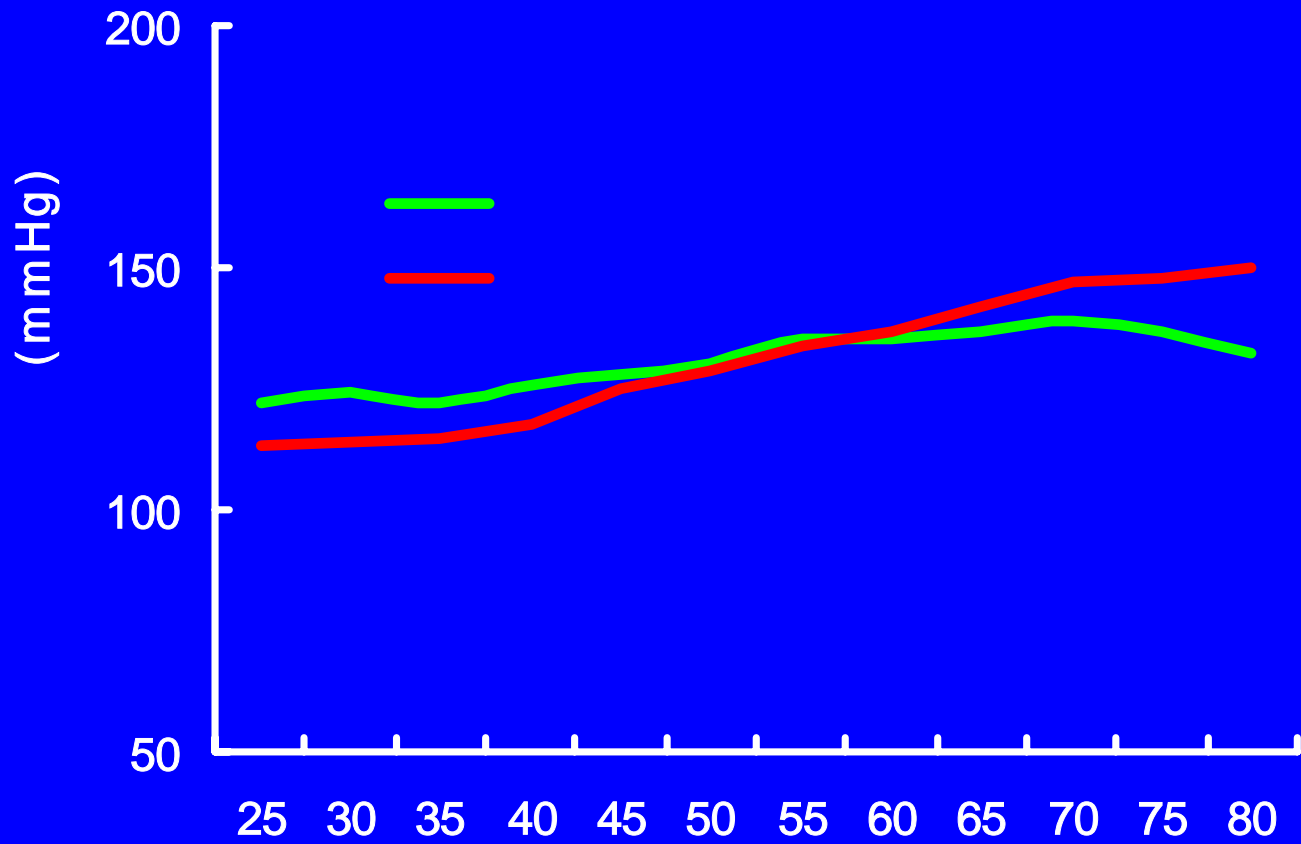
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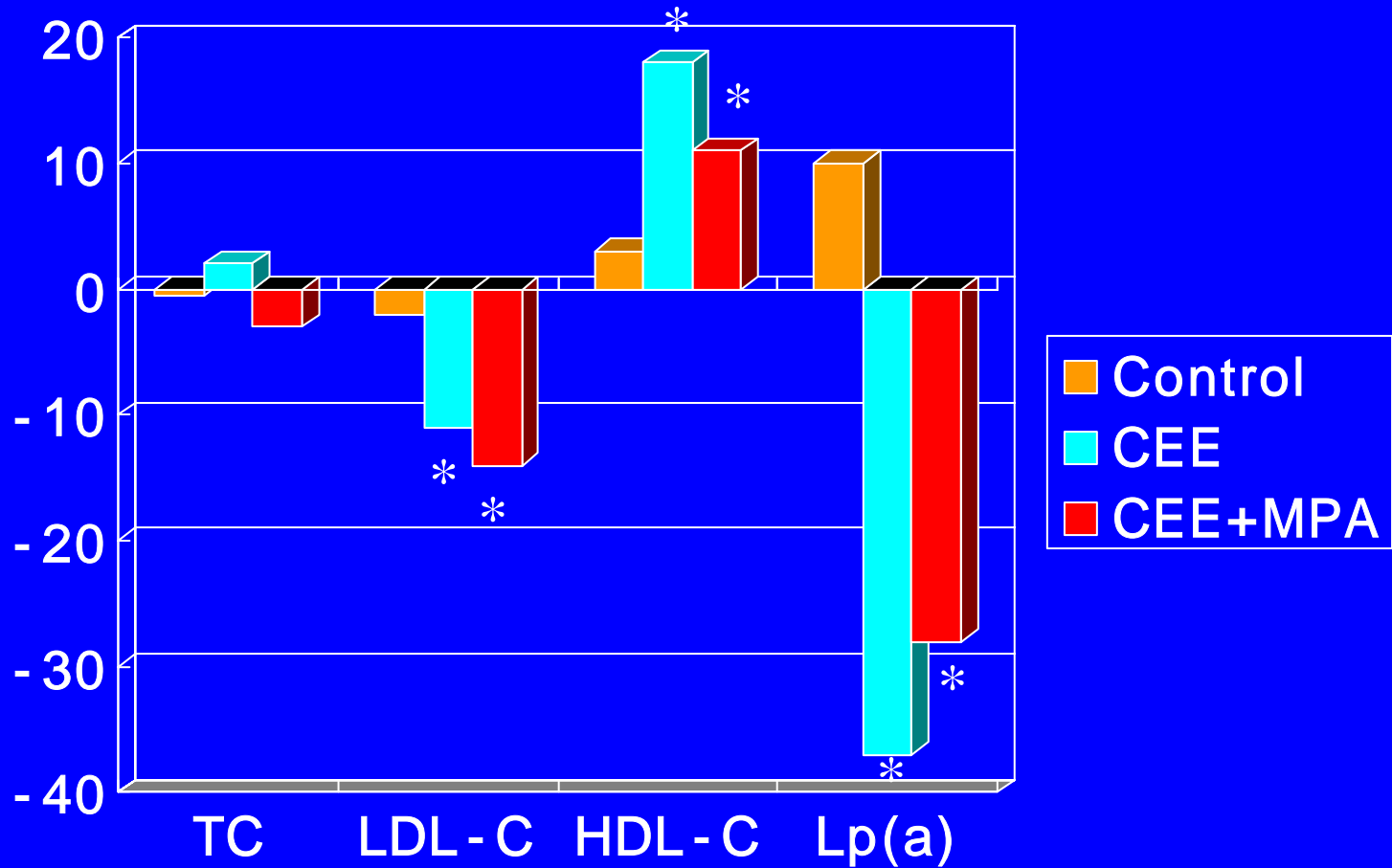
- Improvement of postmenopausal symptoms
 - Prevention of osteoporosis
 - Prevention of cardiovascular diseases (?)

HRT and CHD in Observational Studies

-Summary of 23 Studies-

	Non-user	User	RR
No of patients	1677	593	
CVD death	44	6	
Age-adjusted rate (10000)	38.1	13.1	0.34
Adjusted for age, SBP, smoking			0.37
Education			
< High school	39.6	14.1	
High school	37.0	16.5	
> High school	23.5	8.9	

Effect of HRT on Lipid



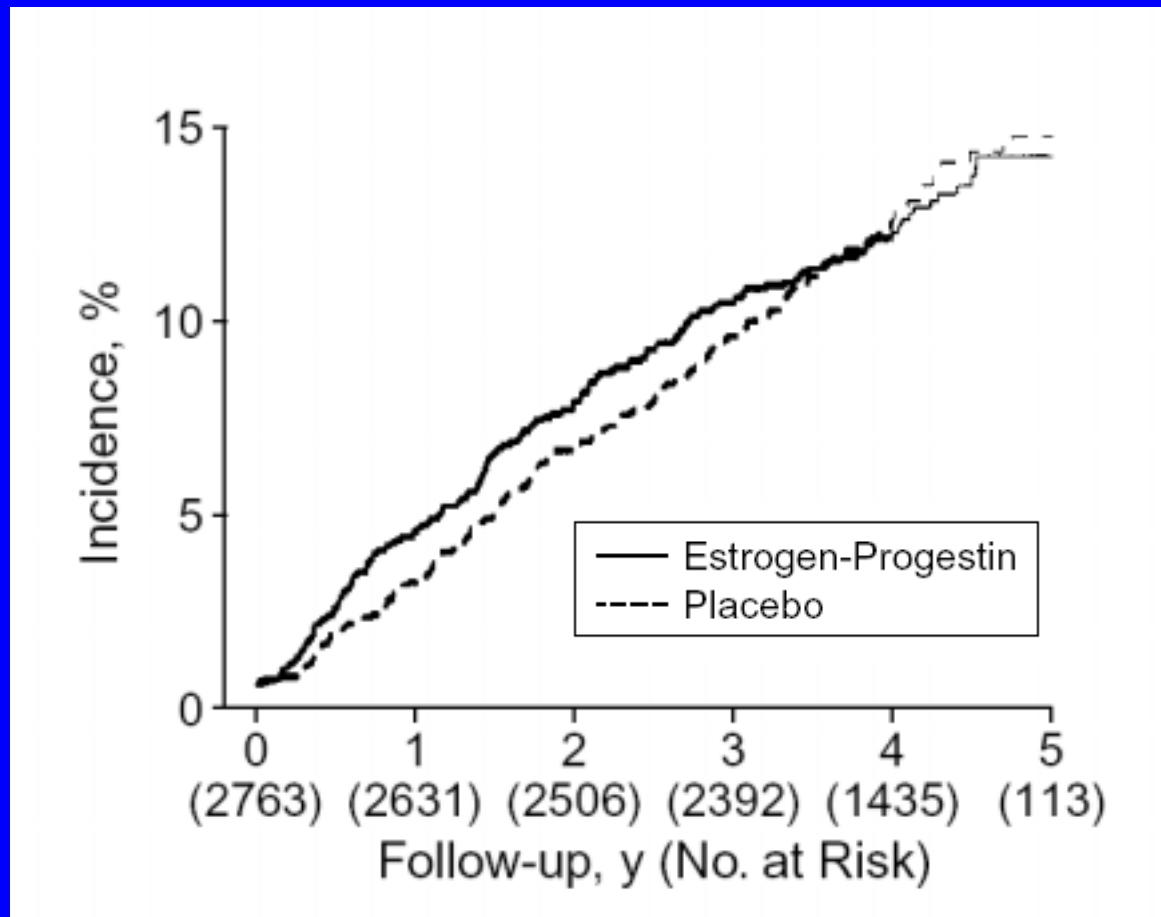
Proposed Mechanisms of ERT for Cardioprotective Effect

- Modification of lipid profiles
 - Reduction of LDL-C and lipoprotein(a)
 - Elevation of HDL-C
- Improving vasoreactivity
- Antioxidant
- Thrombotic & Fibrinolytic mechanism
- Changes in smooth muscle cell and matrix
- Angiogenesis

Heart and Estrogen/progestin Replacement Study (HERS) - CHD

2763 postmenopausal women with CHD < 80 years

0.625 mg of CEE plus 2.5 mg of MPA, Follow-up averaged 4.1 years

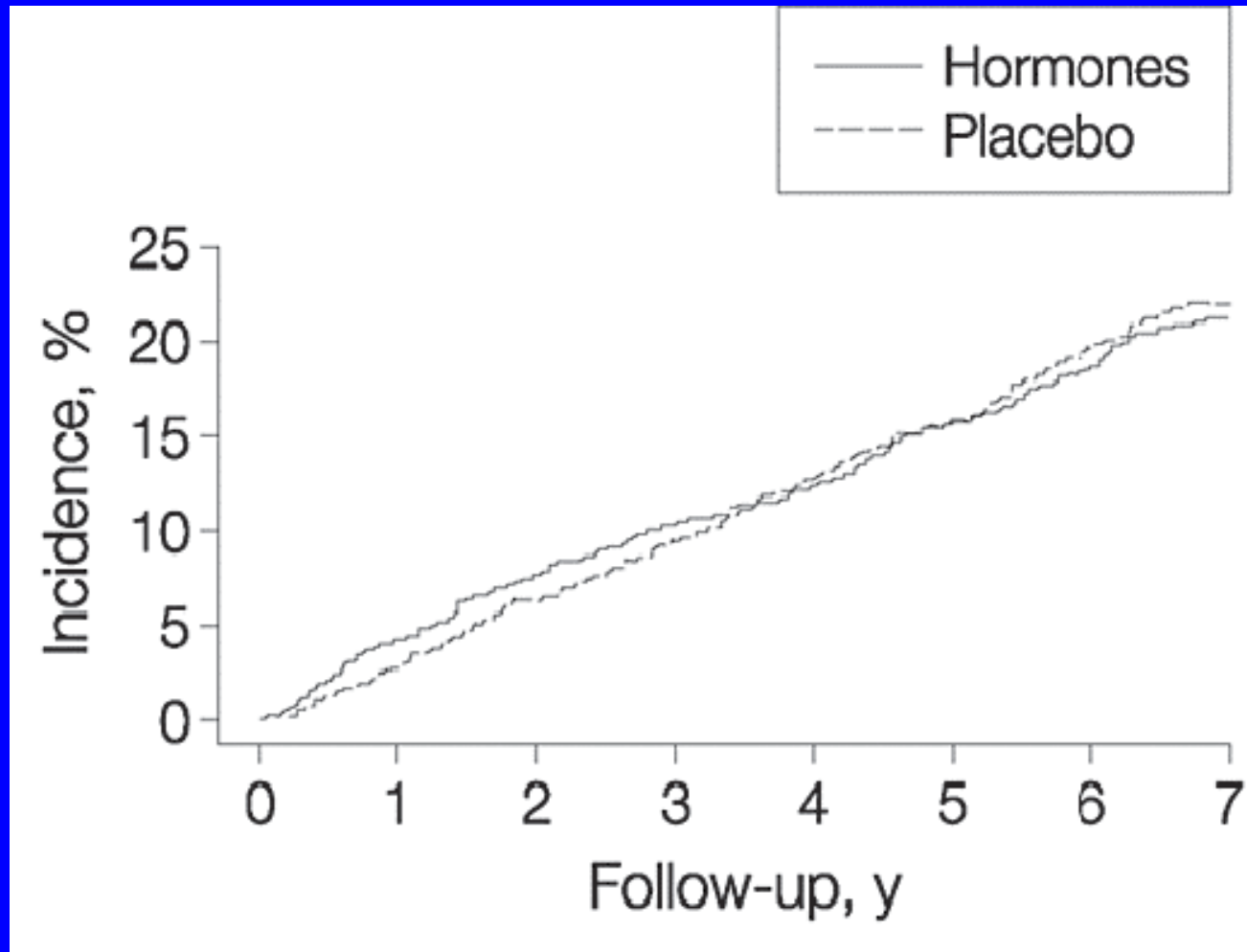


Hypotheses for the HERS Results

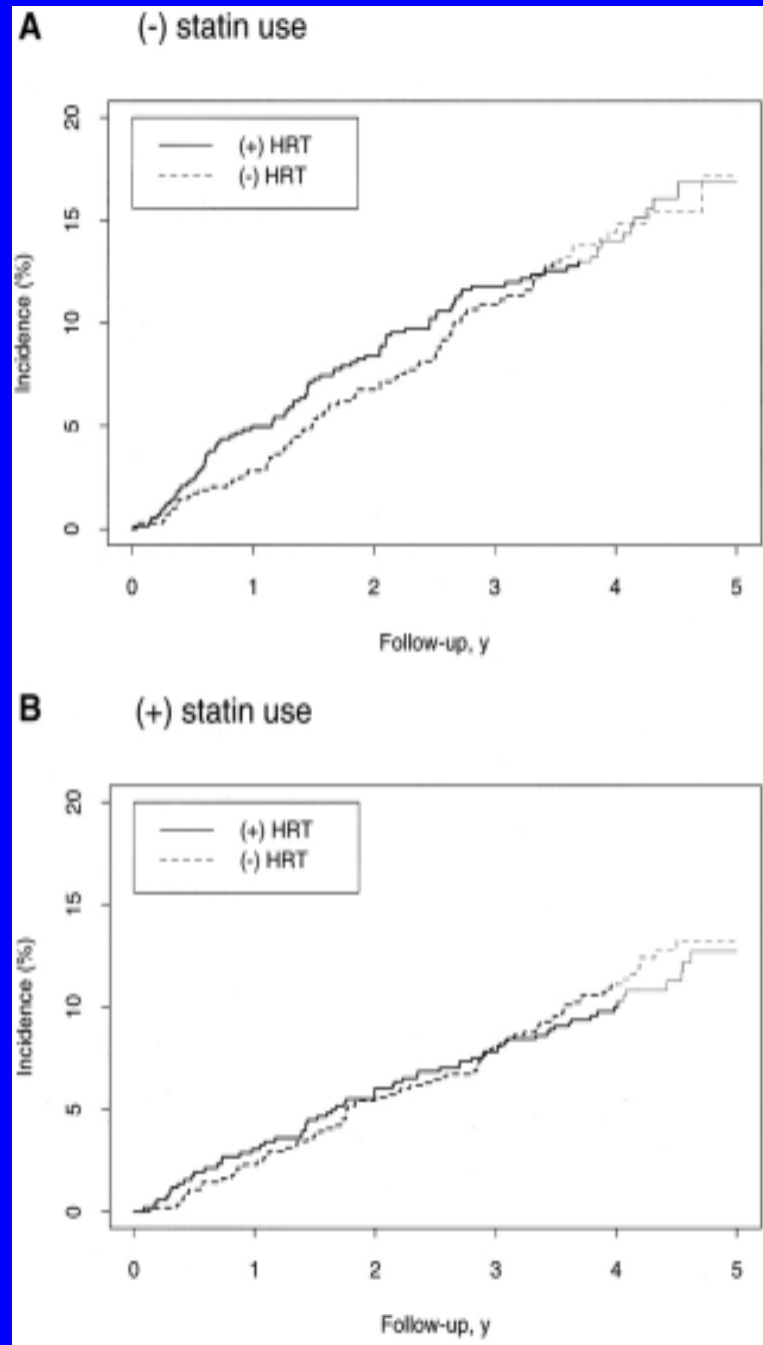
- **Inadequate duration of follow-up**
- **Subjects who were too old**
- **Adverse effect of progesterone**

HRT and Coronary Events

-HERS II-



Effect of Statin CAD Events -HERS-



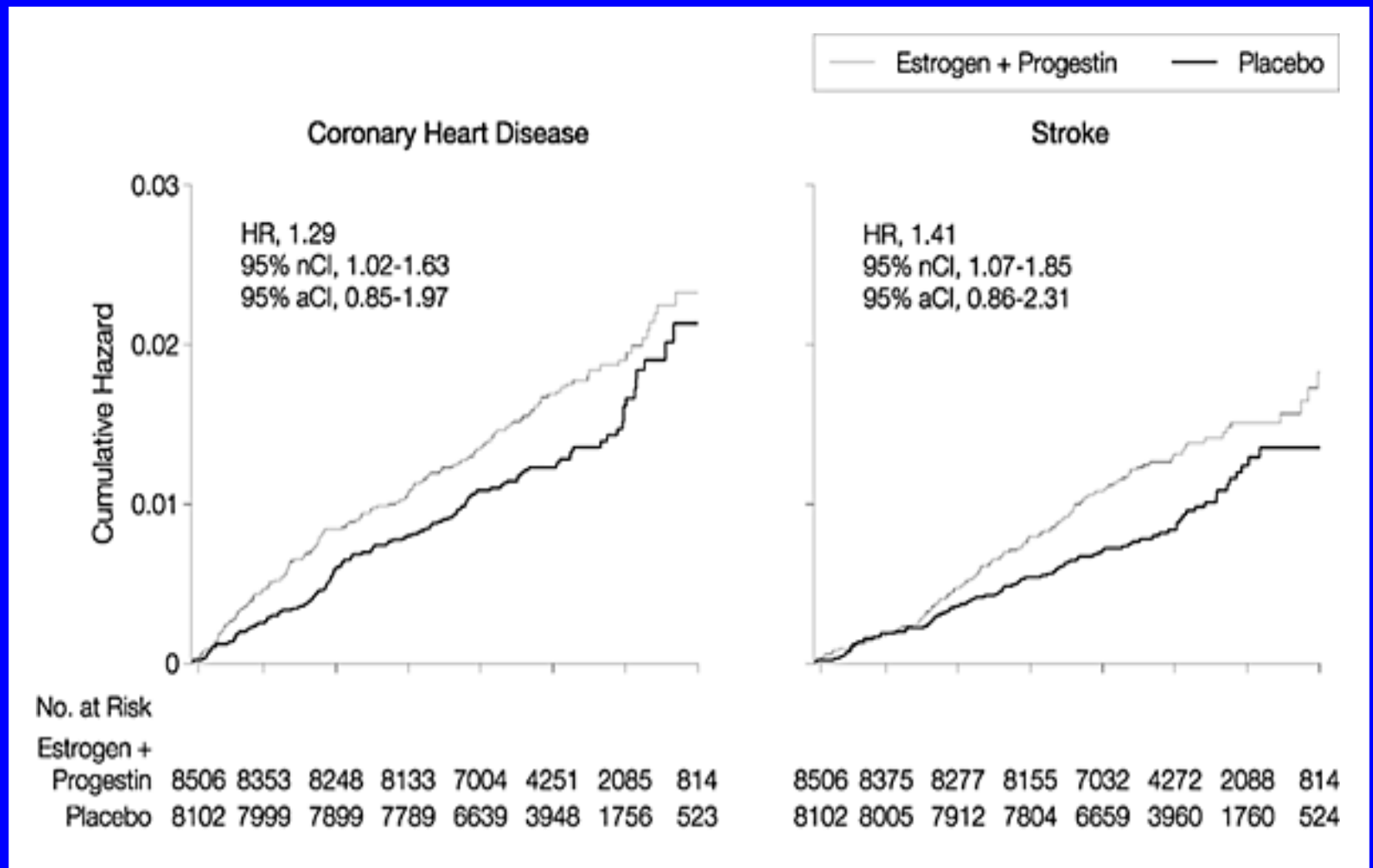
Herrington G. Circulation 2002;105:2962

AHA Recommendations

We said that hormone treatment should not be used to try to prevent a second heart attack or death among women with established heart disease. We'll incorporate the latest findings from the WHI study into our recommendations for women who have no signs of heart disease.

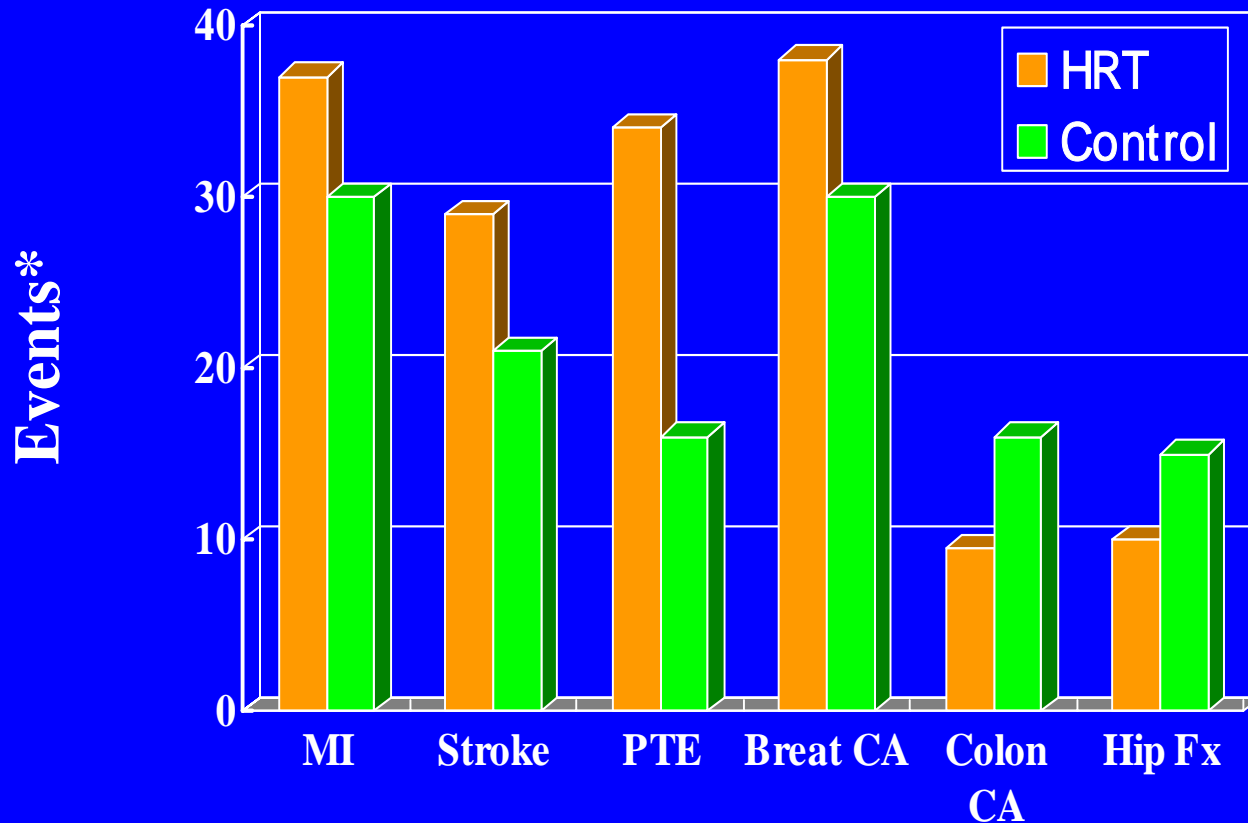
Women's Health Initiative

- WHI-



Absolute Risk of HRT

-WHI-



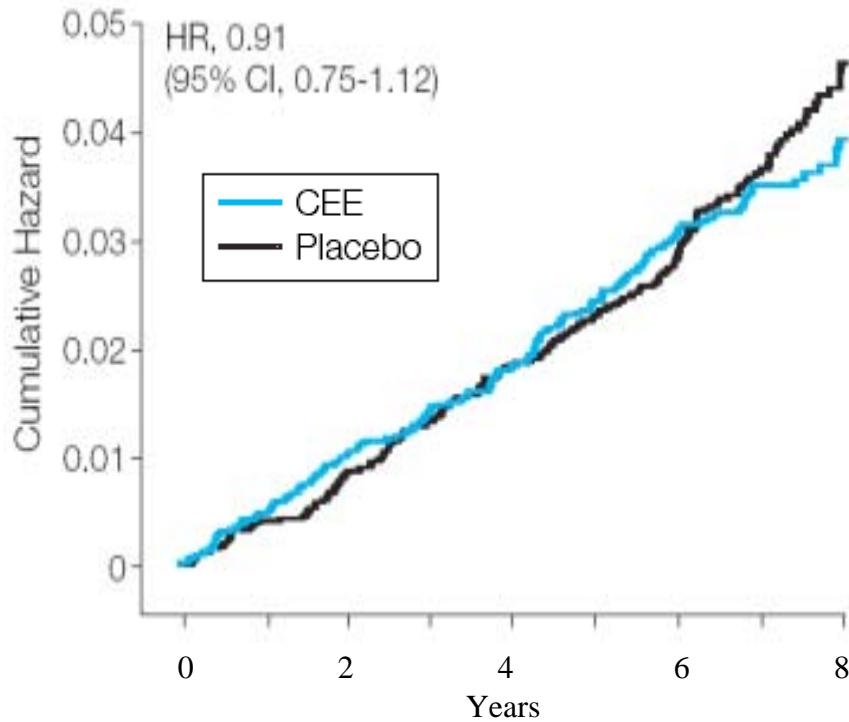
*: Number of events / 10000 women-year

RCTs on HRT

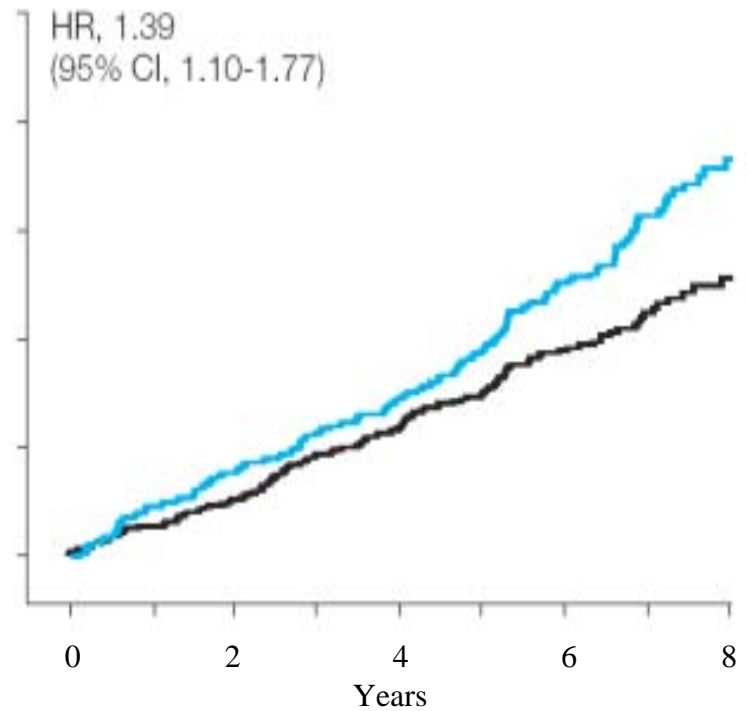
- Women's Atherosclerosis Vitamin/Estrogen Trial (WAVE) - no effect
- Women's Lipid Lowering Heart Atherosclerosis Trial (WELLHART) - no effect
- Estrogen in the Prevention of Atherosclerosis (EPAT) - inhibition of progression of IMT
- Women's Estrogen for Stroke Trial (WEST) - no effect

WHI-Estrogen Arm

Coronary Heart Disease



Stroke



Framingham Study

Estrogen Use	No	Total Death		CHD	
		Actual	Expected	Actual	Expected
< 1 year	120	7	7.1	11	6.5
> 1 year	178	10	10.5	15	9.6

6 year follow up

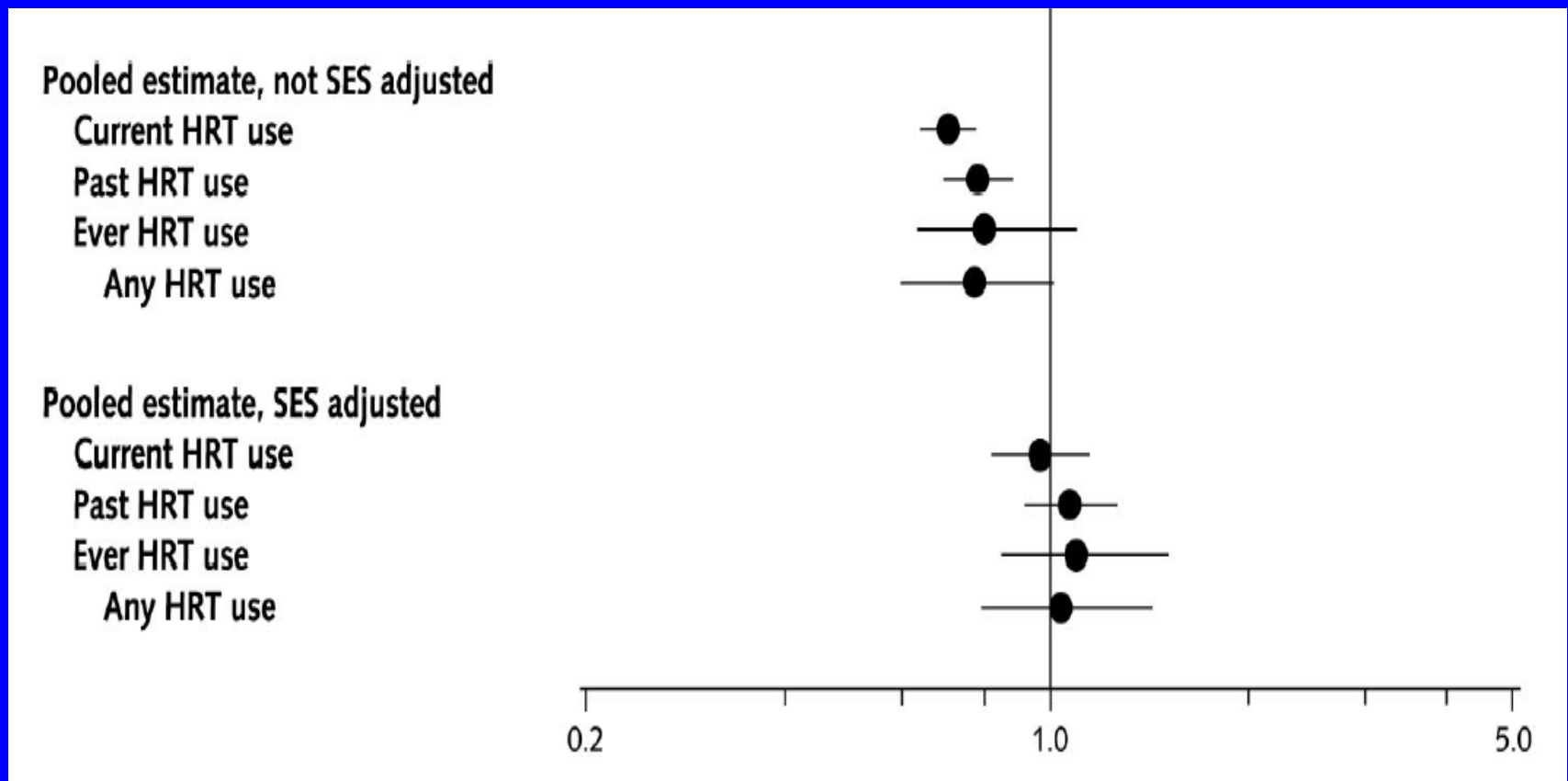
Discrepancy between Observational Studies and RCTs

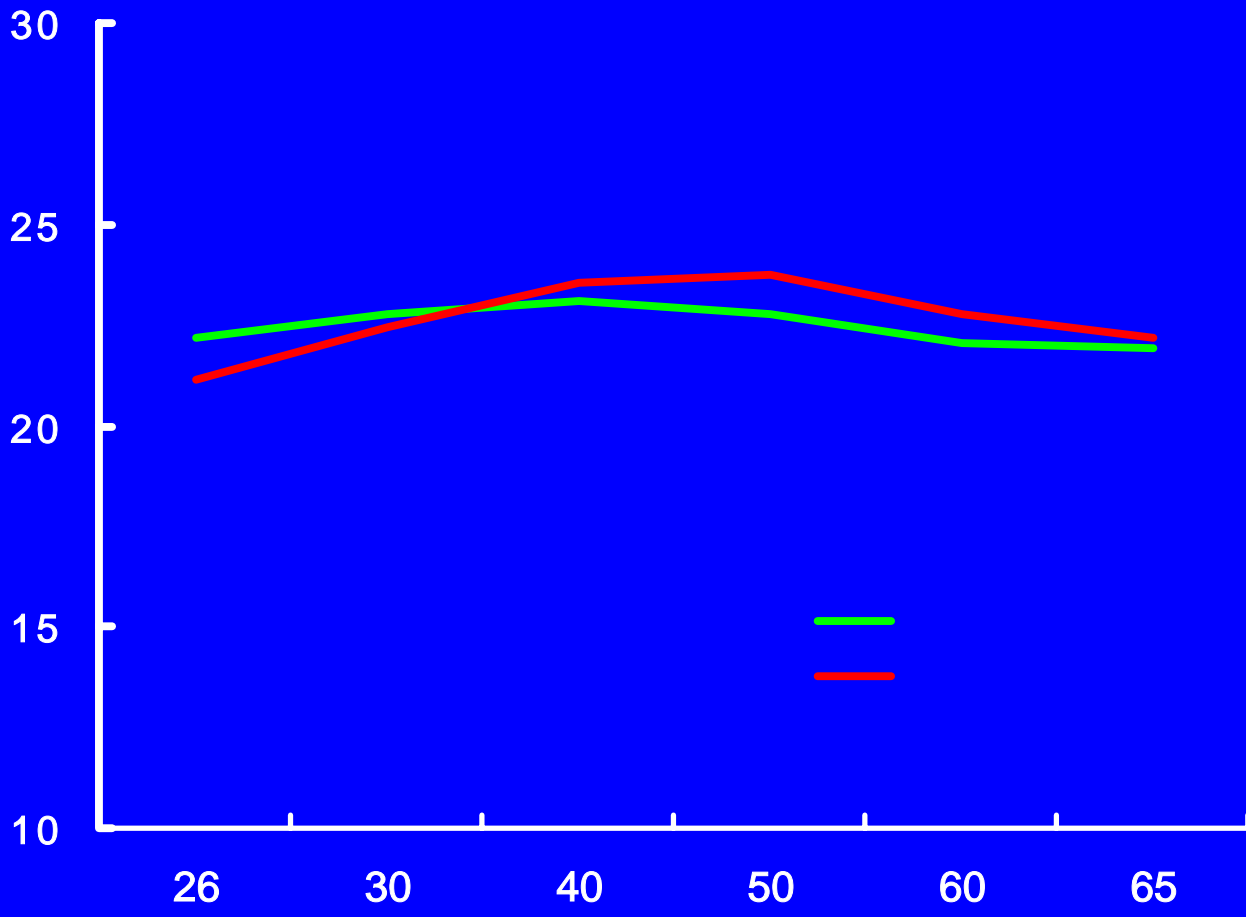
- **HRT user in observational studies**
 - **Healthy**
 - **More educated**
 - **Wealthy**

HRT and CHD in Observational Studies -Meta-analysis of 22 Studies-

Outcome by HRT Use	Relative Risk (95% Confidence Interval)*	Type of Study†	Quality‡
Coronary heart disease			
Incidence			
Current ^{19,30,32-35,37,47,49}	0.80 (0.68-0.95)	RCT, cohort	Fair-good
Current adjusted for socioeconomic status ^{29,34,35,47}	0.97 (0.82-1.16)		
Ever ^{28,29,34,43}	0.91 (0.67-1.33)	Cohort, case control	Fair-good
Past ^{19,30,32,34-36,47}	0.89 (0.75-1.05)	Cohort, case control	Fair-good
All groups ^{19,28-30,32-37,43,47,49}	0.88 (0.64-1.21)	RCT, cohort	Fair-good

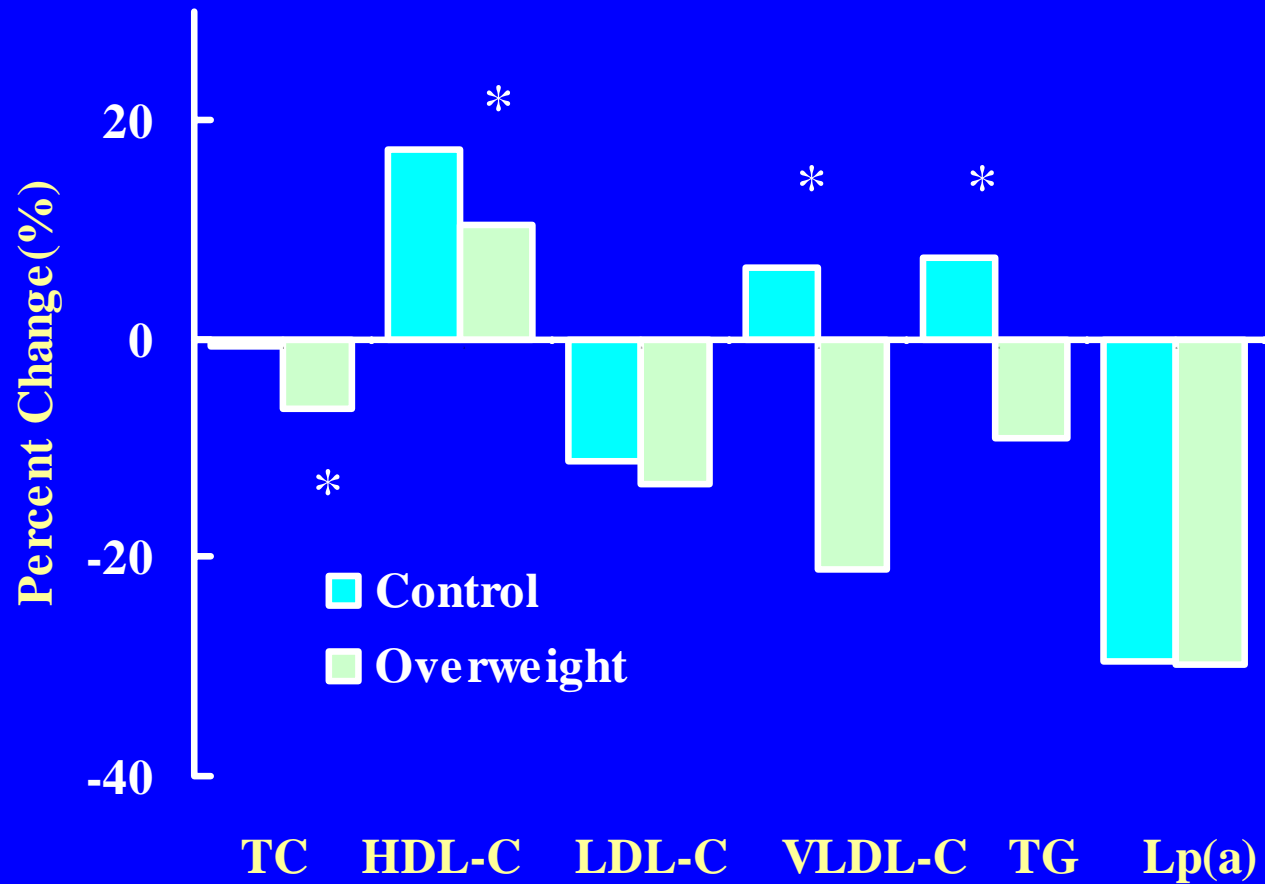
HRT and CHD in Observational Studies -Meta-analysis of 23 Studies-





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Overweight and Effect of HRT on Lipid Profiles

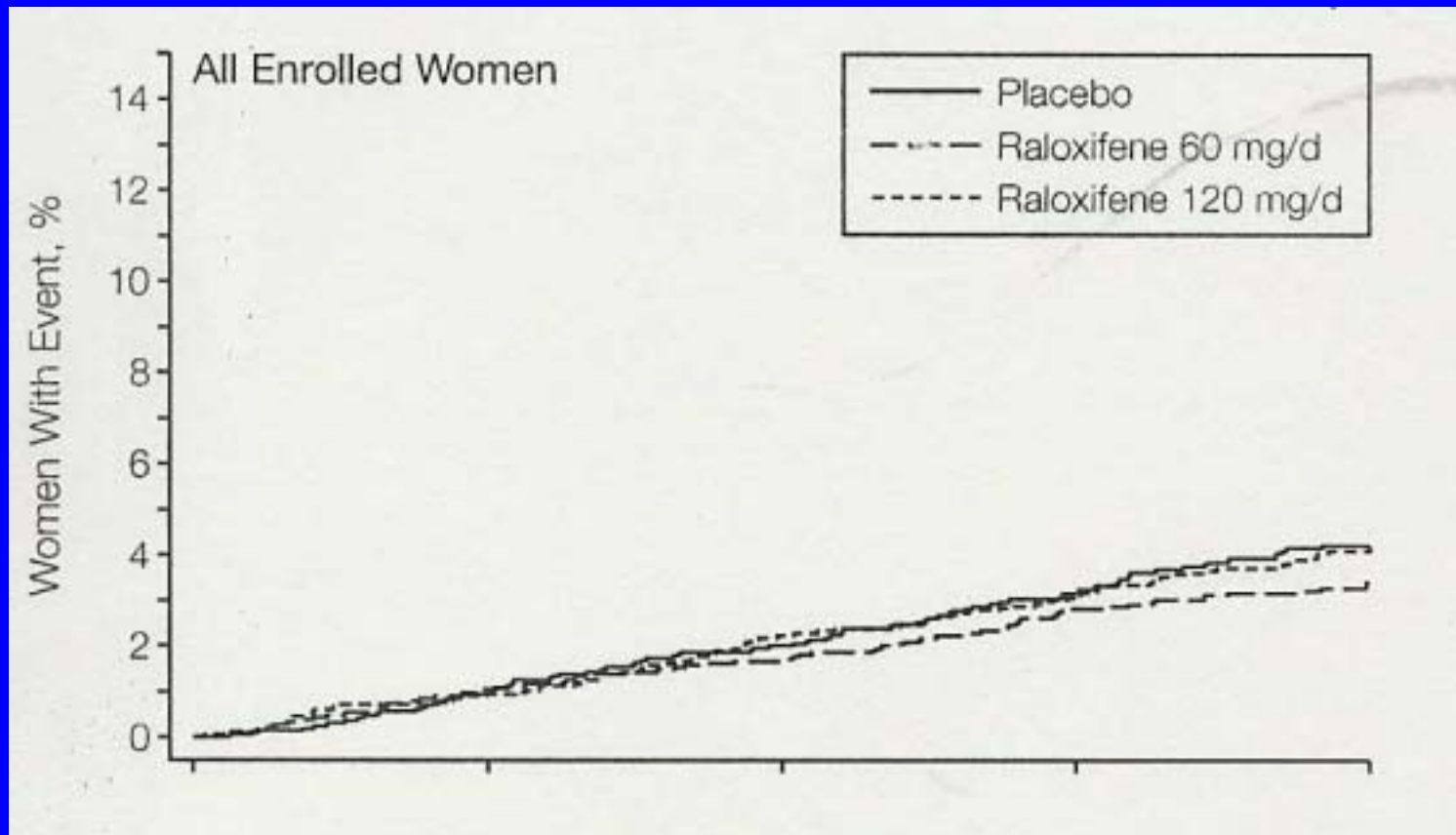


Effect of HRT on Inflammation

Author	Hormones	Study Type	CRP(mg/L)		p value
			Control	Drug	
Ridker(1999)	HRT	CS	0.14	0.27	<0.001
Cushman(1999)	HRT	CS	0.22	0.24	NS
	ERT	CS	0.22	0.35	<0.001
Cushman(1999) (PEPI)	HRT	RCT	0.13	0.25	<0.001
	ERT	RCT	0.13	0.19	<0.001

Multiple Outcomes of Raloxifene Evaluation (MORE)

7705 osteoporotic postmenopausal women
Selective ER modulator, Raloxifene 60 mg or 120 mg
Follow-up averaged 48 months



AHA Recommendations

Selective estrogen receptor modulators (SERMs) aren't the same as HRT. However, like HRT, these should not be used for this purpose until more research is available.

Guidelines for CVD Prevention in Women

-AHA-

Hormone therapy

- Combined estrogen plus progestin hormone therapy should not be initiated to prevent CVD in postmenopausal women. (Class III, Level A)
- Combined estrogen plus progestin hormone therapy should not be continued to prevent CVD in postmenopausal women. (Class III, Level C)
- Other forms of menopausal hormone therapy (eg, unopposed estrogen) should not be initiated or continued to prevent CVD in postmenopausal women pending the results of ongoing trials. (Class III, Level C)

Future Direction for HRT

- New female sex hormones
- Lower dose
- Early administration of hormones
- Route of entry

Effect of Statin CAD Events -HERS-

