V FORUM on **WOMEN, HEALTH,** and **GENDER – Madrid,** October 14-15, 2008

Menopausal Hormone Therapy

The **Women's Health Initiative** (WHI) **randomized, placebo-controlled trials**

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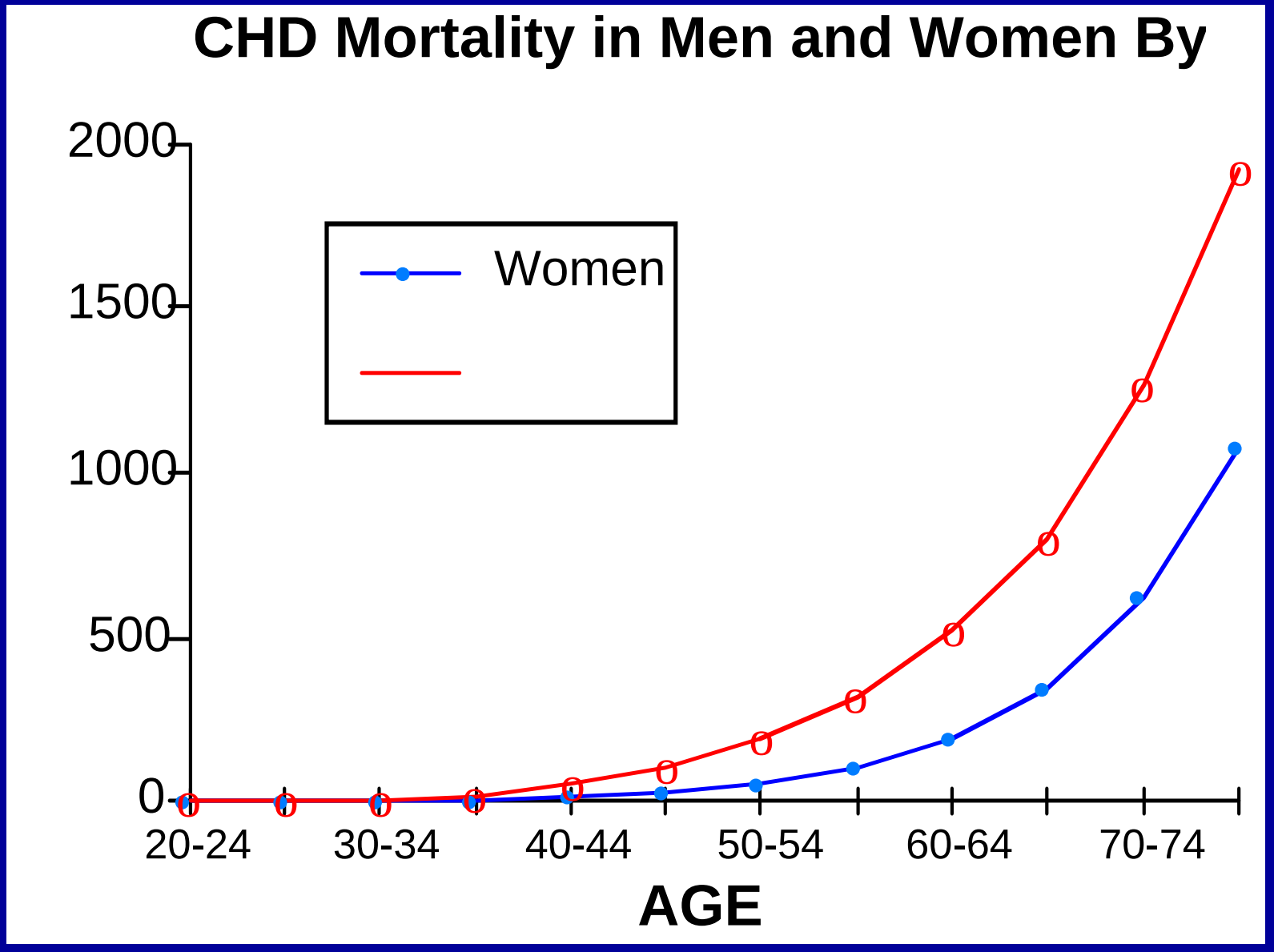
Stanford University School of Medicine


CHD Mortality in Men and Women By
2000
1500
1000
500
0
Women
20-24
30-34
40-44
50-54
60-64
70-74
AGE

CHD Mortality in Men and Women by Age

Myth and paradox of coronary risk and menopause

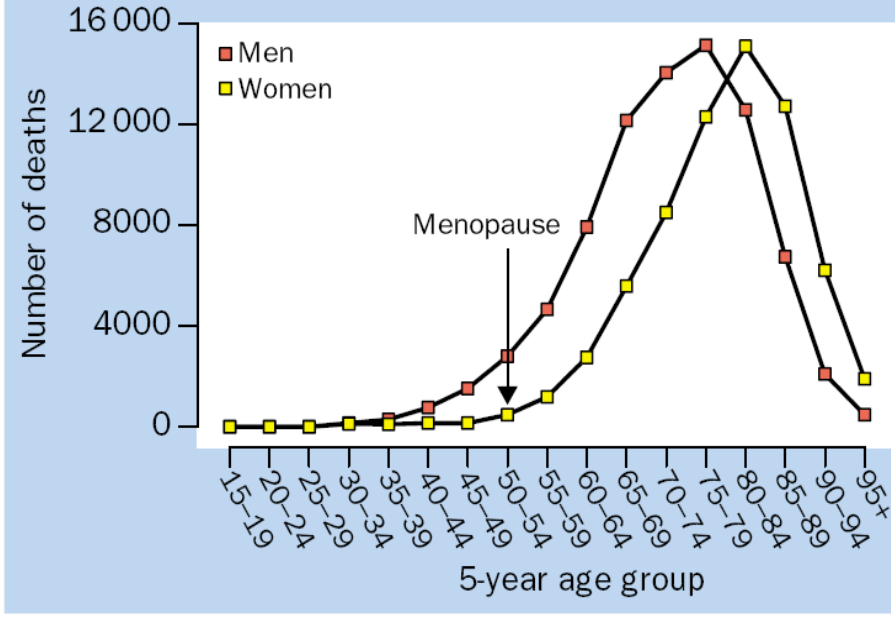


Figure 1: **Numbers of coronary deaths by age and sex**

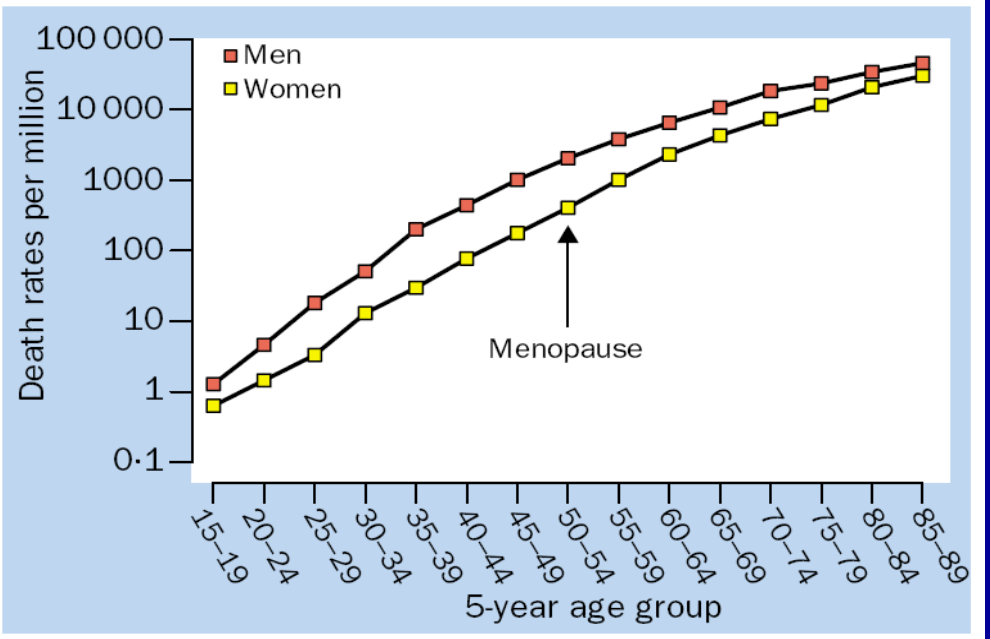
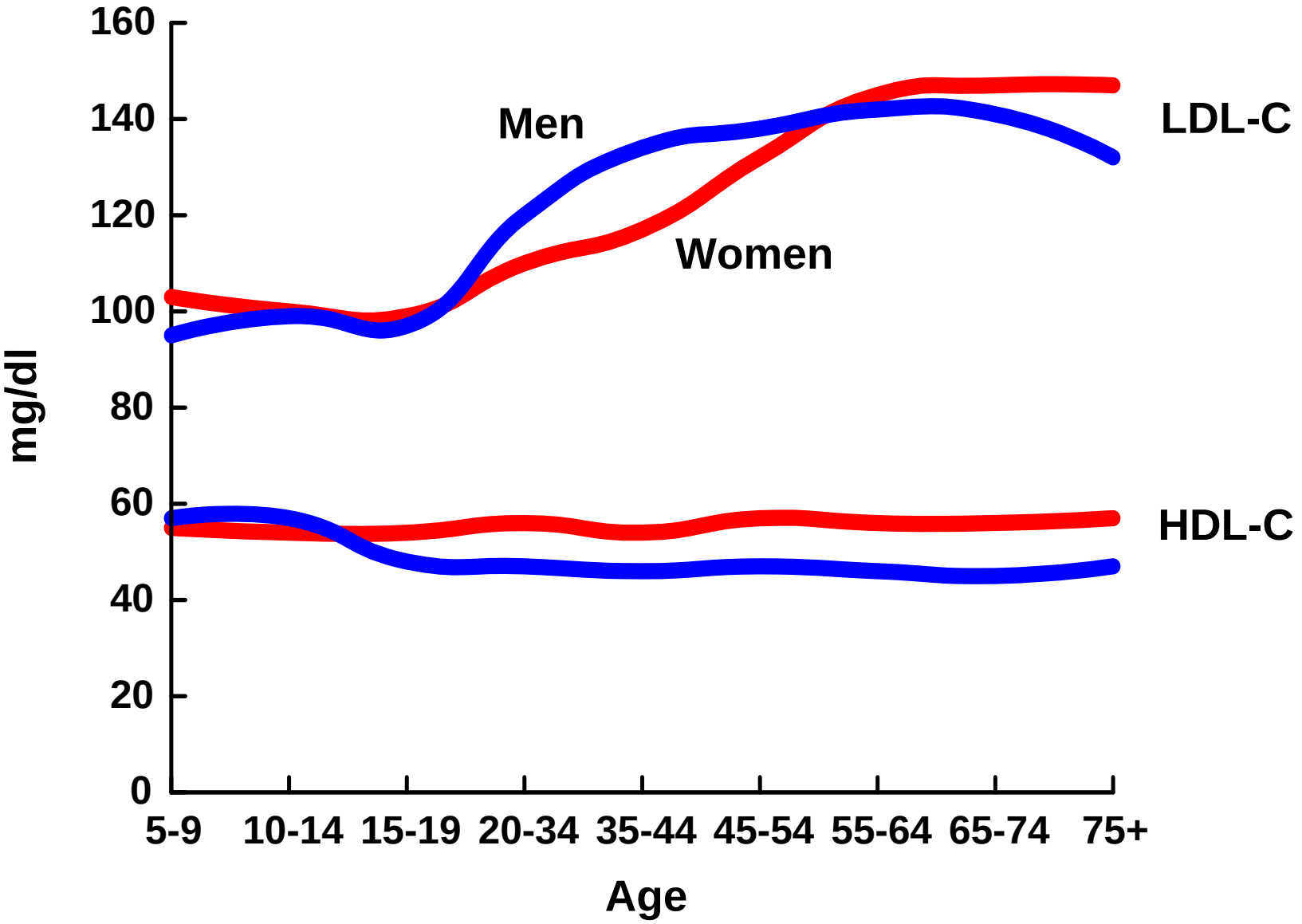


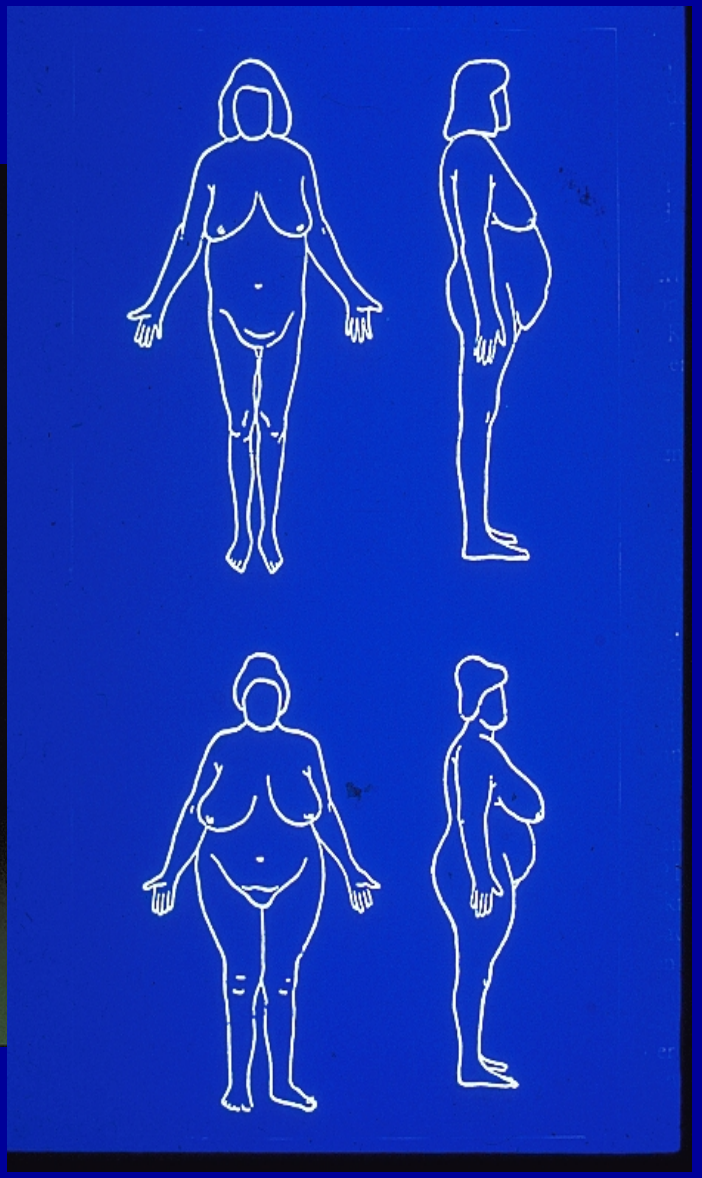
Figure 2: **Death rates per million by age and sex (logarithmic scale)**

Tunstall-Pedoe, Lancet 1998; 351: 1425-27

Lipid Levels by Age and Sex

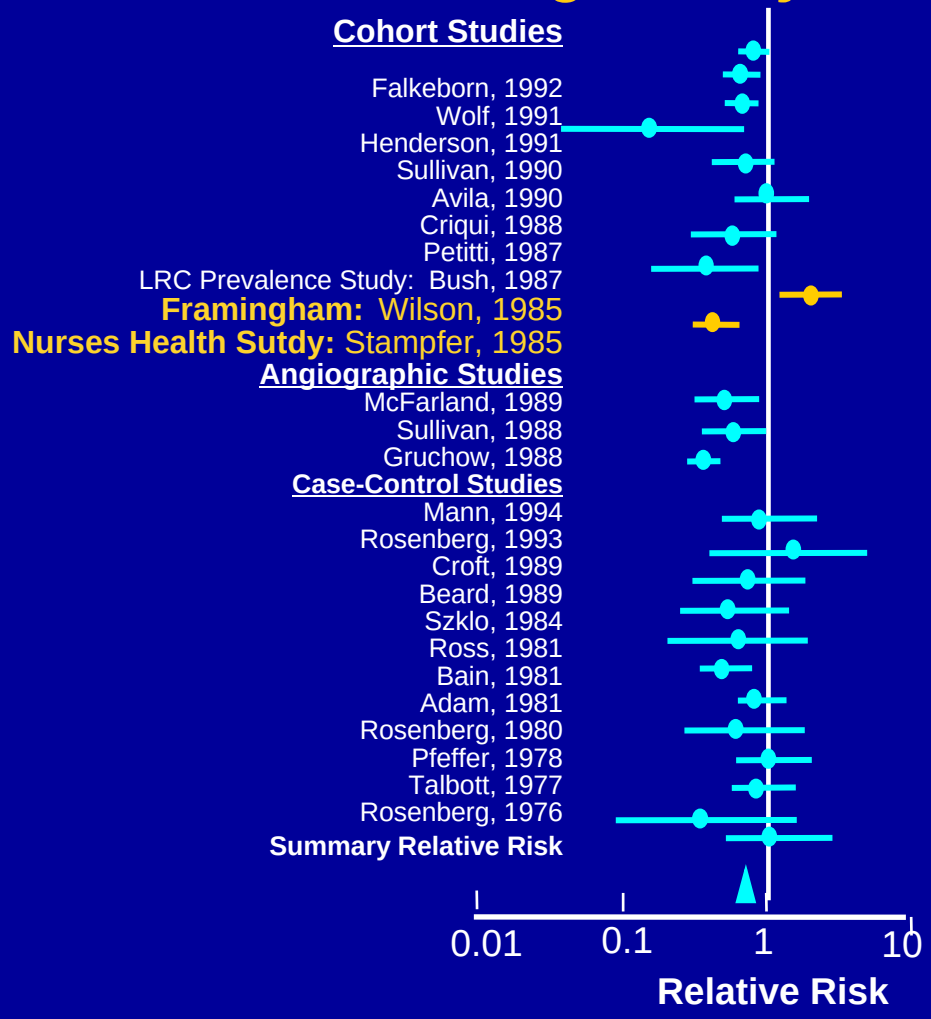
LRC Prevalence Study



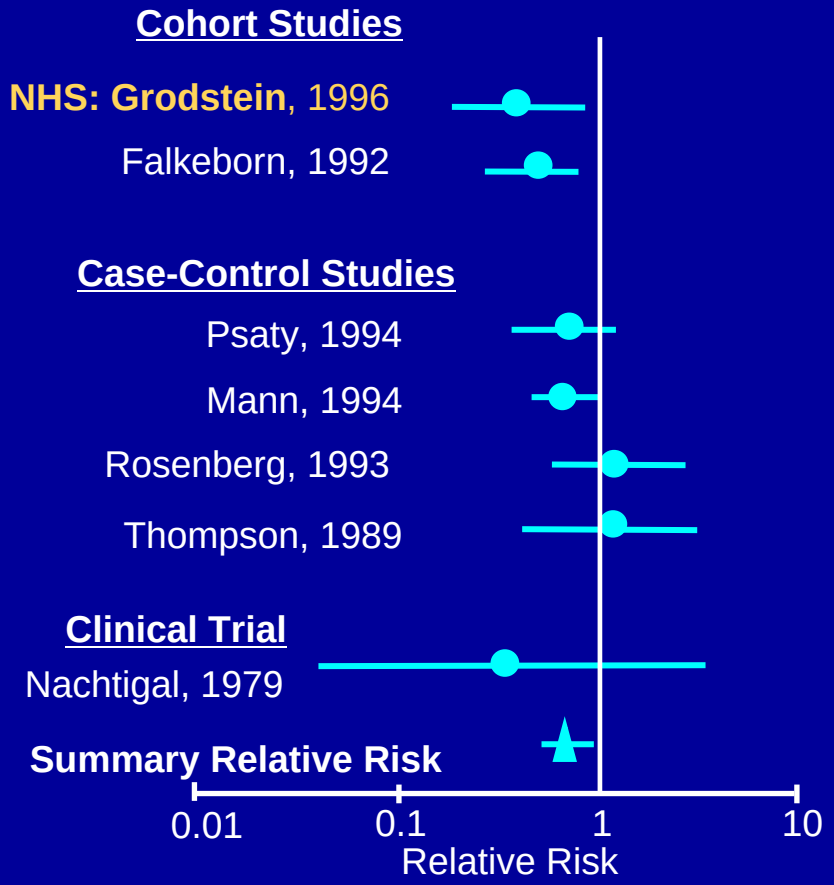


Risk for CHD: Hormone Users vs. Nonusers

Estrogen Only



Estrogen+ Progestin



Barrett-Connor. **Annu Rev Public Health. 1998;19:55-72**

PEPI

Postmenopausal Estrogen-Progestin Interventions

- 875 postmenopausal women, aged 45-64, low CHD risk
- 3 years - *too small & too short to study actual heart disease*
- randomized (women with & without uterus) to:
  - (1) Placebo
  - (2) Conjugated Equine Estrogens (CEE), 0.625 mg/day
  - (3) CEE + cyclic Medroxyprogesterone Acetate (MPA), 10 mg/d 1-12
  - (4) CEE + daily MPA, 2.5 mg/day
  - (5) CEE + cyclic Micronized Progesterone, 200 mg/days 1-12
- CHD Risk:
  - Favorable: HDL-C [E > E+P], LDL-C, Lp(a); Fibrinogen
  - Neutral: Blood Pressure, Insulin
  - Unfavorable: Triglycerides, C-Reactive Protein*
- Bone Mineral Density improved

JAMA 1995; 273: 199-208 * Circulation 1999; 100: 717-722

HERS

Heart and Estrogen-Progestin Replacement Study

- **2763 women (with uterus),** aged < 80 yrs**, with heart disease**
- **4.1 years - Primary outcome: Fatal and Non-fatal heart disease**
- **randomized to:** CEE + daily MPA (Prempro®) **- or - Placebo**

- **HT(E+P)** increased **HDL-C**, reduced **LDL-C**, increased **TG** vs placebo
- **No difference in overall rate of CHD events by 4.1 yrs**
- CEE+MPA**: more heart attacks in 1st yr (RR=1.52)**
  - **Blood Clots (VTE), Lungs (PE) & Legs (DVT), increased 3-fold.**
  - **Slight increase in gallbladder disease**.
  - No difference in **fracture**, cancer, total mortality (limited power)

Hulley S et al JAMA 1998; 280: 605-13; Ann Intern Med 2000; 132: 689-696

HERS-II (extended follow-up)

- **No difference in overall CHD events by ~ 7 yrs** *(Grady D, et al. JAMA. 2002;288:58-66)*

Hormone Trials: Secondary CVD prevention

Trial	Treatment	N	Endpoint	Outcome
HERS	**CEE + MPA**	**2763**	**Events**	**Early harm, No benefit** (cardiac, stroke, PVD)
ERA	**CEE ±MPA**	**309**	**Angiogram**	**No benefit**
WEST	**17b-estradiol**	**664**	**Stroke**	**Early harm, No benefit**
PHASE	**transdermal 17b-estradiol + norethisterone**	**225**	**Events** (stopped 4yrs)	**Possible early harm No benefit**
WAVE ± Vitamins	**CEE ±MPA**	**423**	**Angiogram No benefit**	**Possible harm;**
HERS-II	***CEE+MPA***	***2321***	***Events***	***No benefit***
WELL-HART ±MPA	**17b-estradiol**	**226**	**Lesions**	**No benefit**

The **Protective Effect of Estrogen** on the **Cardiovascular System.** - *Mendelsohn ME, Karas RH.* ***N Engl J Med 1999; 340: 1801-11.***

- **Estrogen receptors:** α and **ß**
  - **Vascular endothelial and smooth muscle cells bind E with high affinity**
- **Lipoproteins** (account for ~1/3 of observed clinical benefits of E therapy)
  - **HDL increased** by estrogens, blunted by Progestin ***(Oral > Transdermal)***
  - **LDL & LP(a) decreased** by estrogens ***(Oral > Transdermal)***
    Triglycerides increased by estrogens
- **Systemic Effects**
  - **Coagulation and Fibrinolytic Systems** ***(Oral > Transdermal)***
  - **Antioxidant Systems**
  - **Production of Vasoactive Molecules,** e.g. nitric oxide, prostaglandins
- **Actions on Blood Vessels - affects vasomotor tone**
  - **Vasodilation increased** by estrogens (NO-related effect)
    - **5-10 min** after E administered, **not dependent on gene expression**
  - **Inhibition of response to vascular injury**
    - **over a period of hours or days, dependent on gene expression**
    - accelerates endothelial cell growth, inhibits aptosis
    - Promotes migration and proliferation of smooth muscle cells

Funded by National Institutes of Health

Women's Health Initiative (WHI) Clinical Trials

(Diet, Hormones, Calcium/Vit D)
and Observational Study

Conducted at 40 Clinical Centers
+ Clinical Coordinating Center
(Fred Hutchinson Cancer Research Center)

www.whi.org

www.whiscience.org

WHI Clinical Trials: Sample Size, Key Outcomes; Criteria: Postmenopausal Women, aged 50-79; Not moving < 3 yrs

Diet Modification (DM) Trial

Primary Outcomes:

Breast & Colorectal Cancer

Secondary Outcome:

Coronary Heart Disease (CHD)

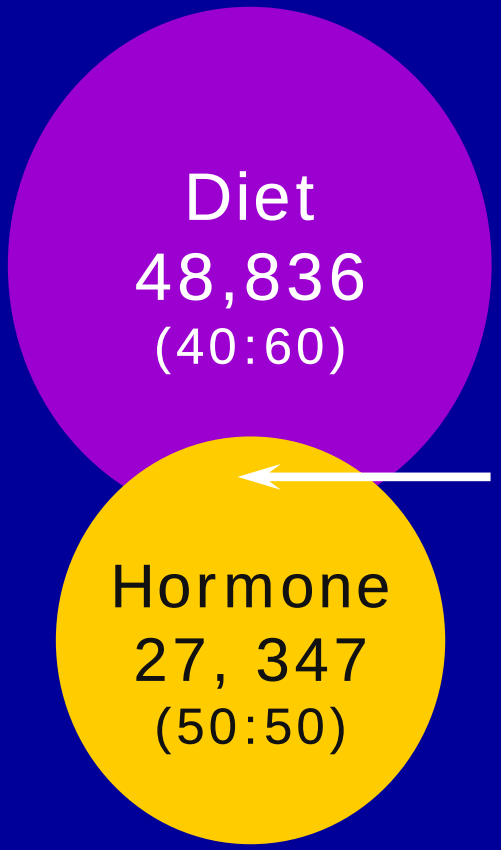
Hormone Trials

Primary Outcome: CHD

Secondary Outcomes:

Hip Fracture, Breast Cancer

Ancillary Study: Memory (Dementia)



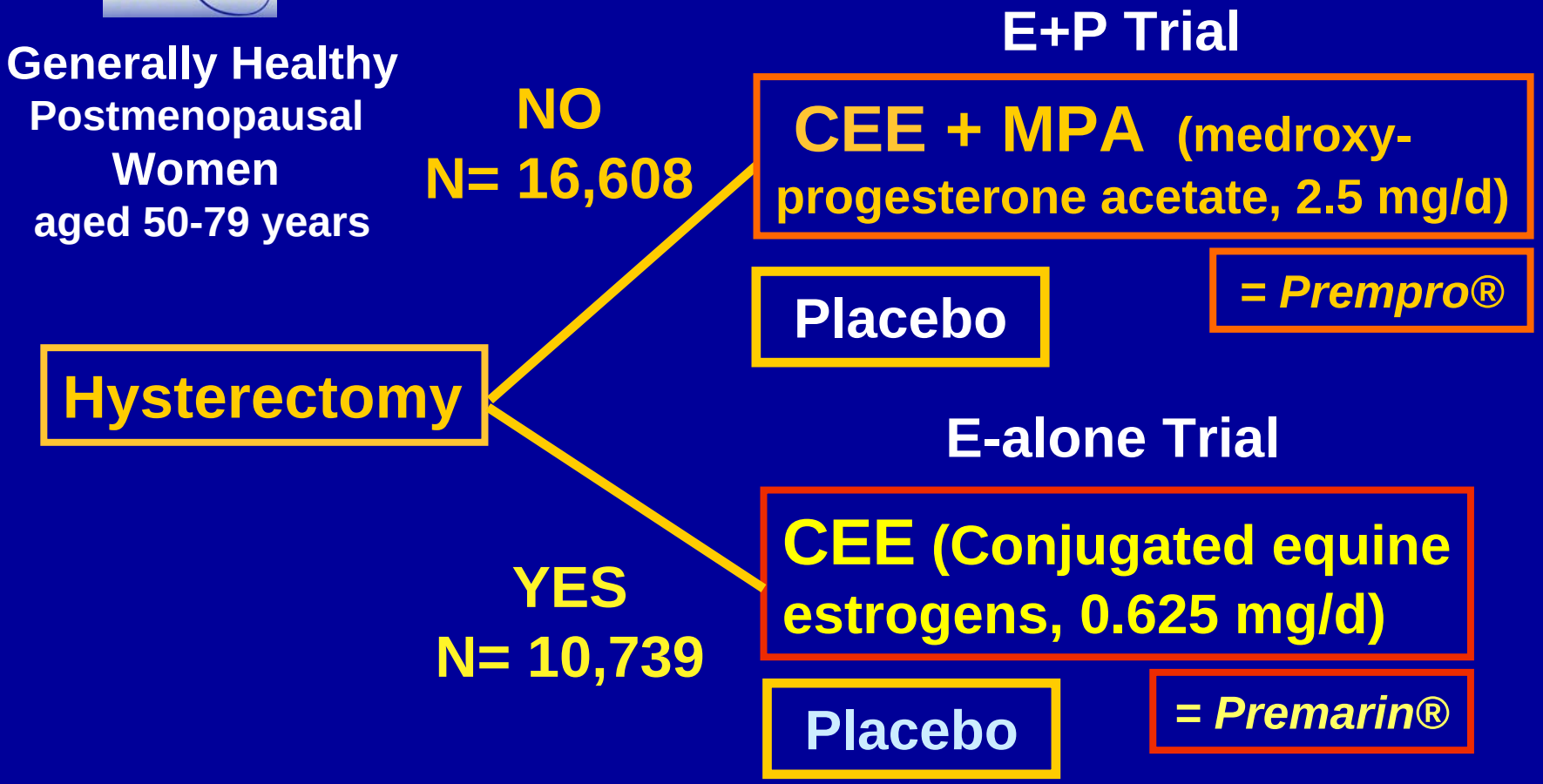
Design
~ 9 years
average
follow-up

11.8%
Overlap

Total CT = 68,133

WOMEN'S HEALTH INITIATIVE

Women's Health Initiative (WHI)
Hormone Therapy (HT) Trials



*Initially: CEE only (N=331), CEE+□MPA, or Placebo
(Post-PEPI: CEE only were converted to CEE+MPA)

Current HT required 3-month wash-out before baseline testing.

WHI Hormone Therapy (HT) Trials

(27,347 Postmenopausal Women, aged 50-79, at baseline**)**

HT (E+P & E-Alone) Trials

Primary Outcome:

Coronary Heart Disease

Secondary Outcomes:

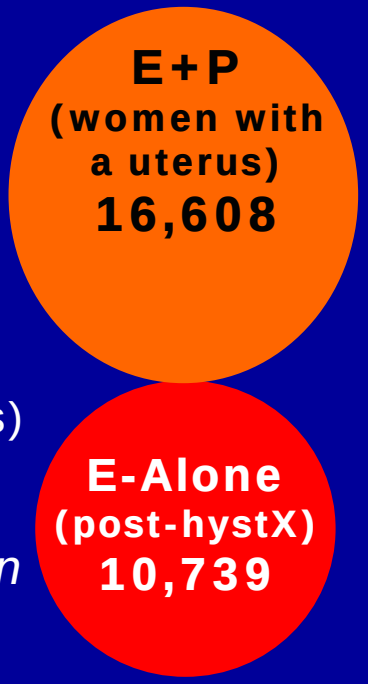
Stroke, Blood Clots

- **Lungs** (**PE**, pulmonary emboli)
- Legs (DVT, deep vein thrombosis)

Cancer: **Breast, Colorectal, Endometrial** (Uterine), *Ovarian*

Hip Fracture; Other Deaths

WHI Memory Study (WHIMS)
***- for women aged ≥ 65*: Dementia**

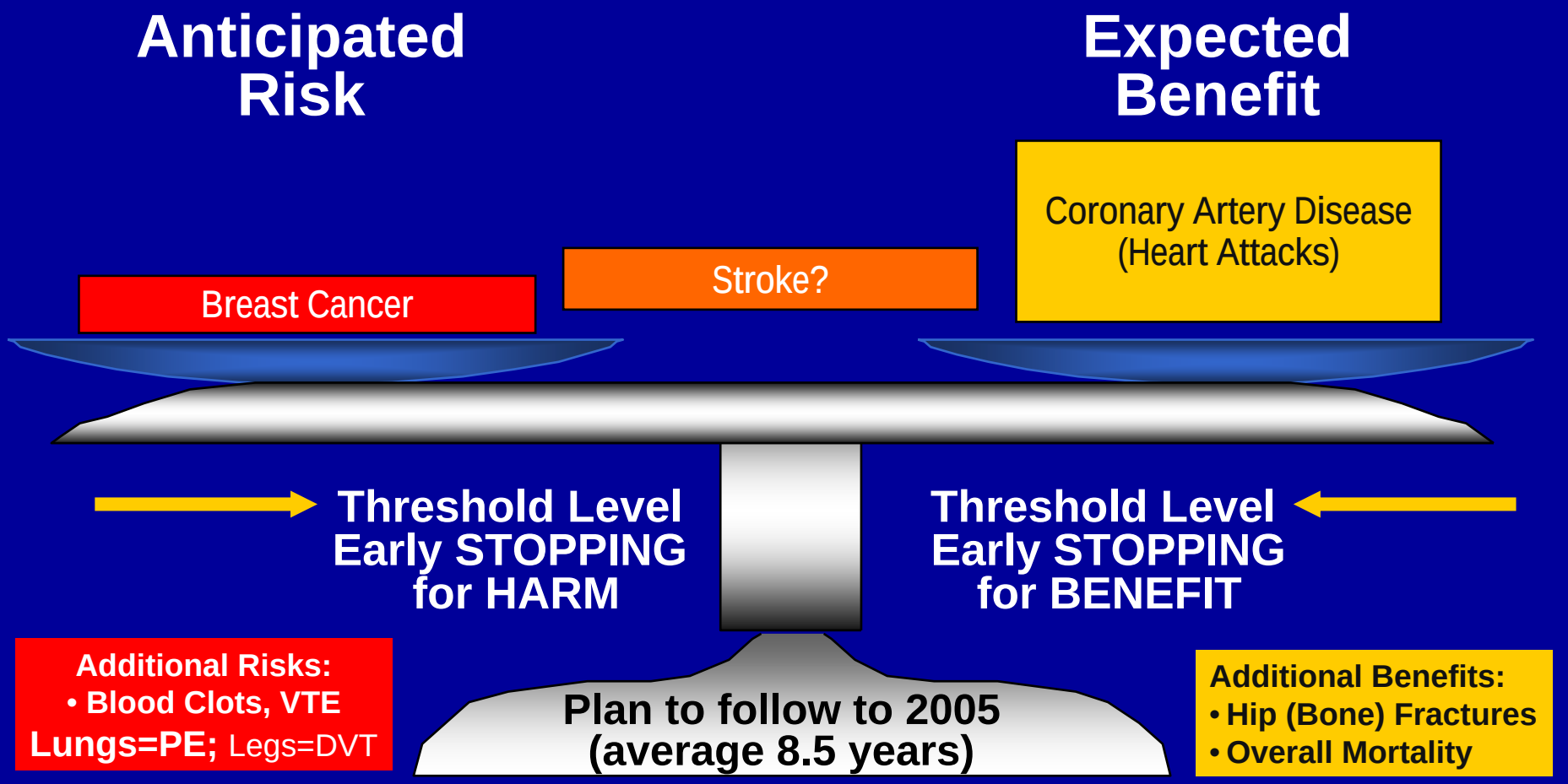


Average Follow-up 5.6 years*

Average 7.1 years*

***design ~ 8.5 years**

WHI Hormone Trials: Baseline Hypotheses

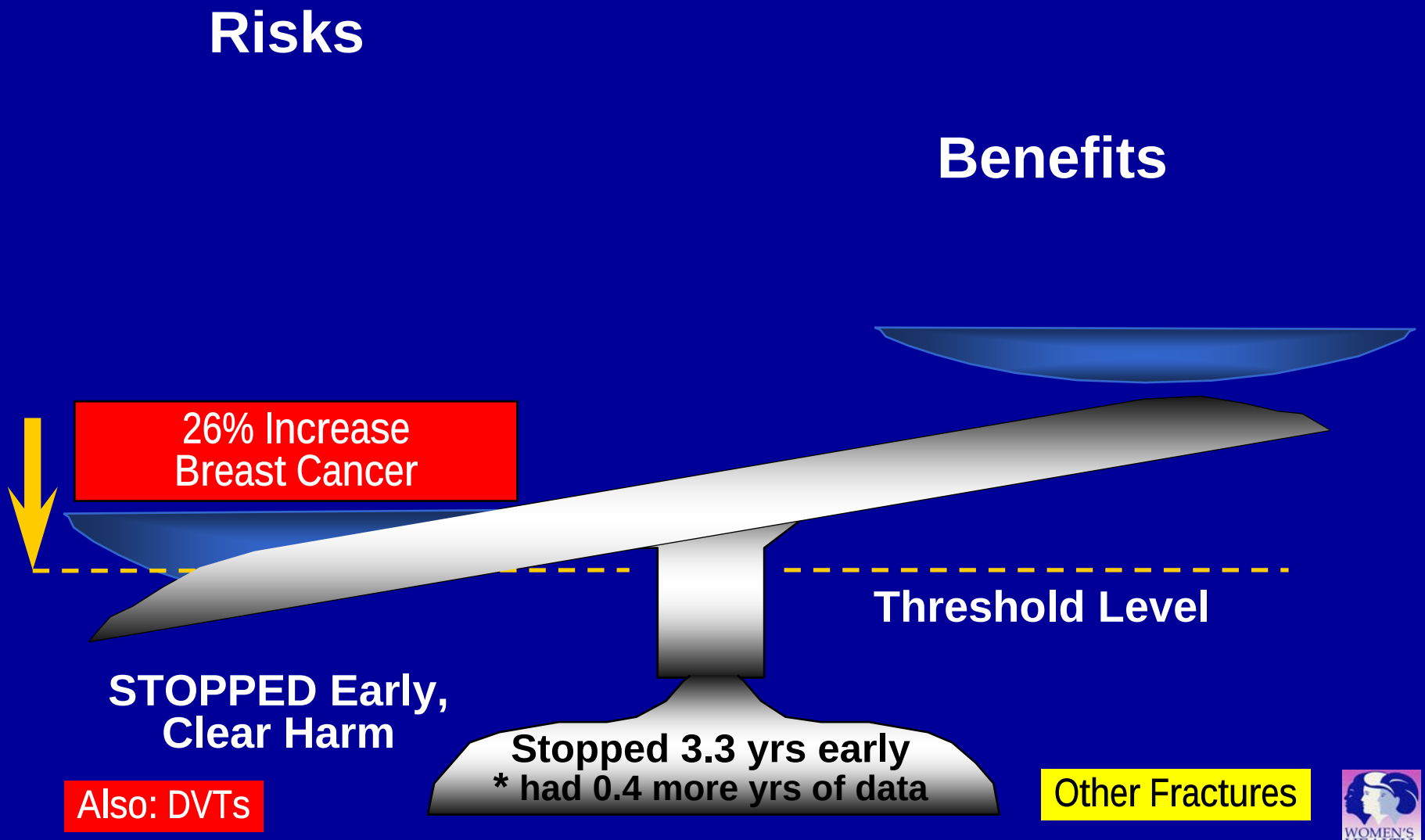


- **Global Index: overall balance of benefits and risks**

  Earliest occurrence of **CHD, Stroke, PE, Breast Cancer, Hip Fracture, Colorectal Cancer, Death from other causes,** Endometrial Cancer

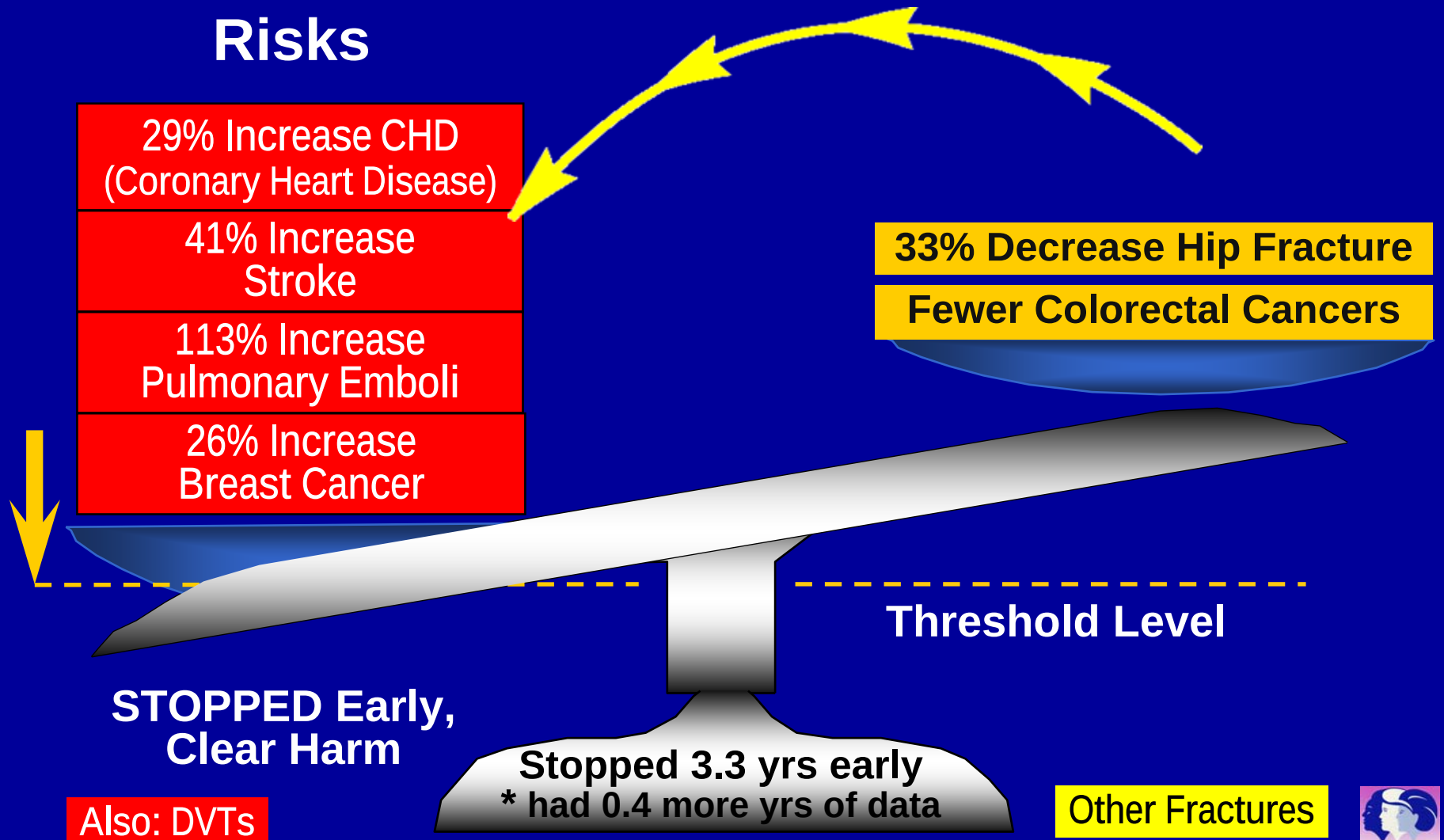
WOMEN'S HEALTH INITIATIVE

WHI E+P Trial: Preliminary Findings, July 2002 (aver. 5.2 yrs)



*Adapted from: Writing Group for the Women's Health Initiative. **JAMA. 2002;288:321-333**

WHI E+P Trial: Preliminary Findings, July 2002 (aver. 5.2 yrs)



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WHI E+P Trial: Participant Retention

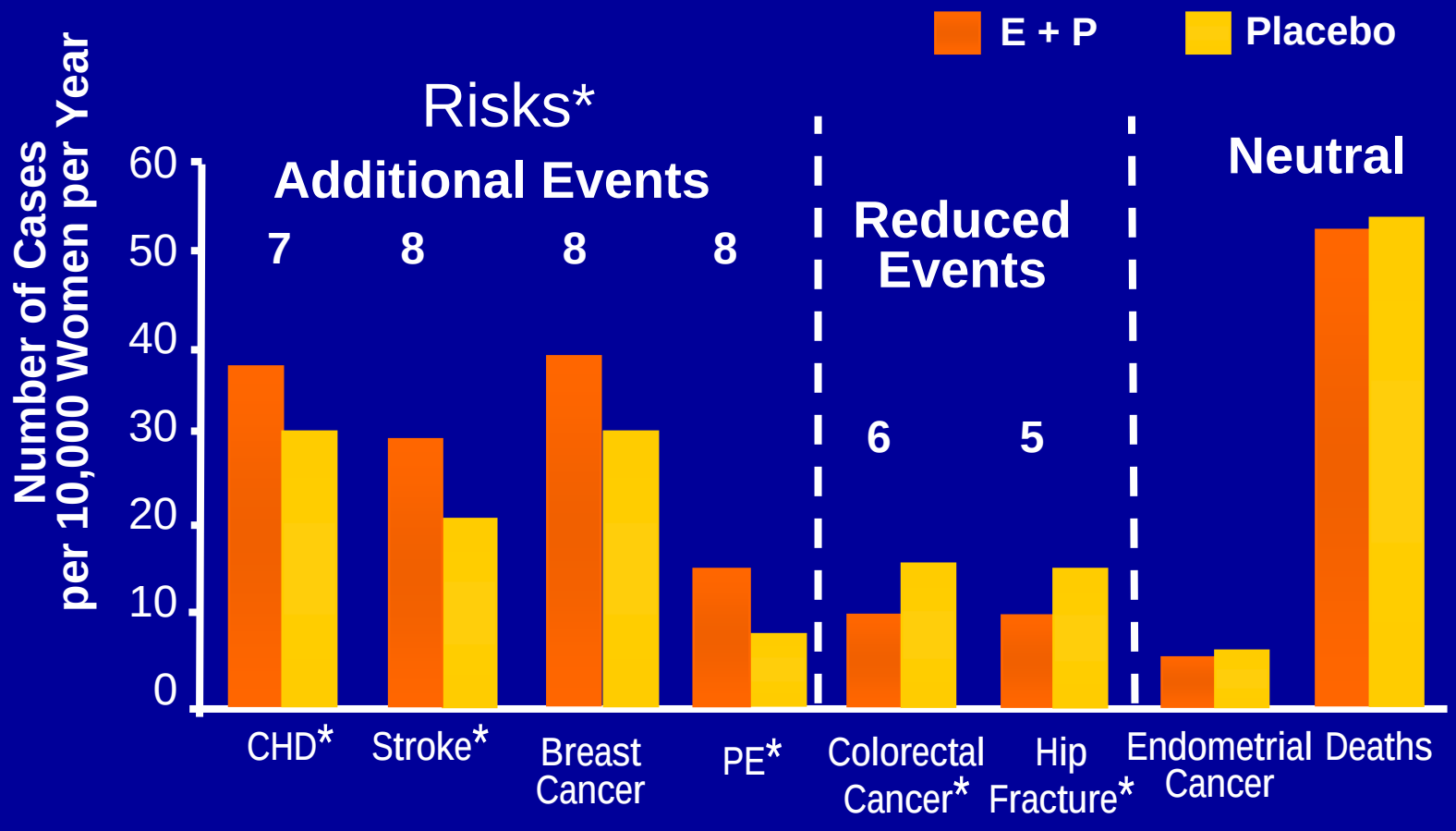
16,608 Randomized

CEE+MPA (N = 8506)			Placebo (N = 8102)		
Status on 04/30/02 (aver. 5.6 yrs)			**Status on 04/30/02 (aver. 5.6 yrs)**		
Alive & Outcomes data submitted in last 18 months	(n = 7968)	**93.7%**	**Alive & Outcomes data submitted** in last 18 months	(n = 7608)	**93.9%**
Unknown Vital Status	(n = 307)	**3.6%**	**Unknown Vital Status**	(n = 276)	**3.4%**
Deceased	(n = 231)	**2.7%**	**Deceased**	(n = 218)	**2.7%**

Writing Group for the Women's Health Initiative Steering Committee: **JAMA 2002; 288: 321-333**

WHI E+P Trial: Absolute (annualized) Risk (5.2 Yrs*)

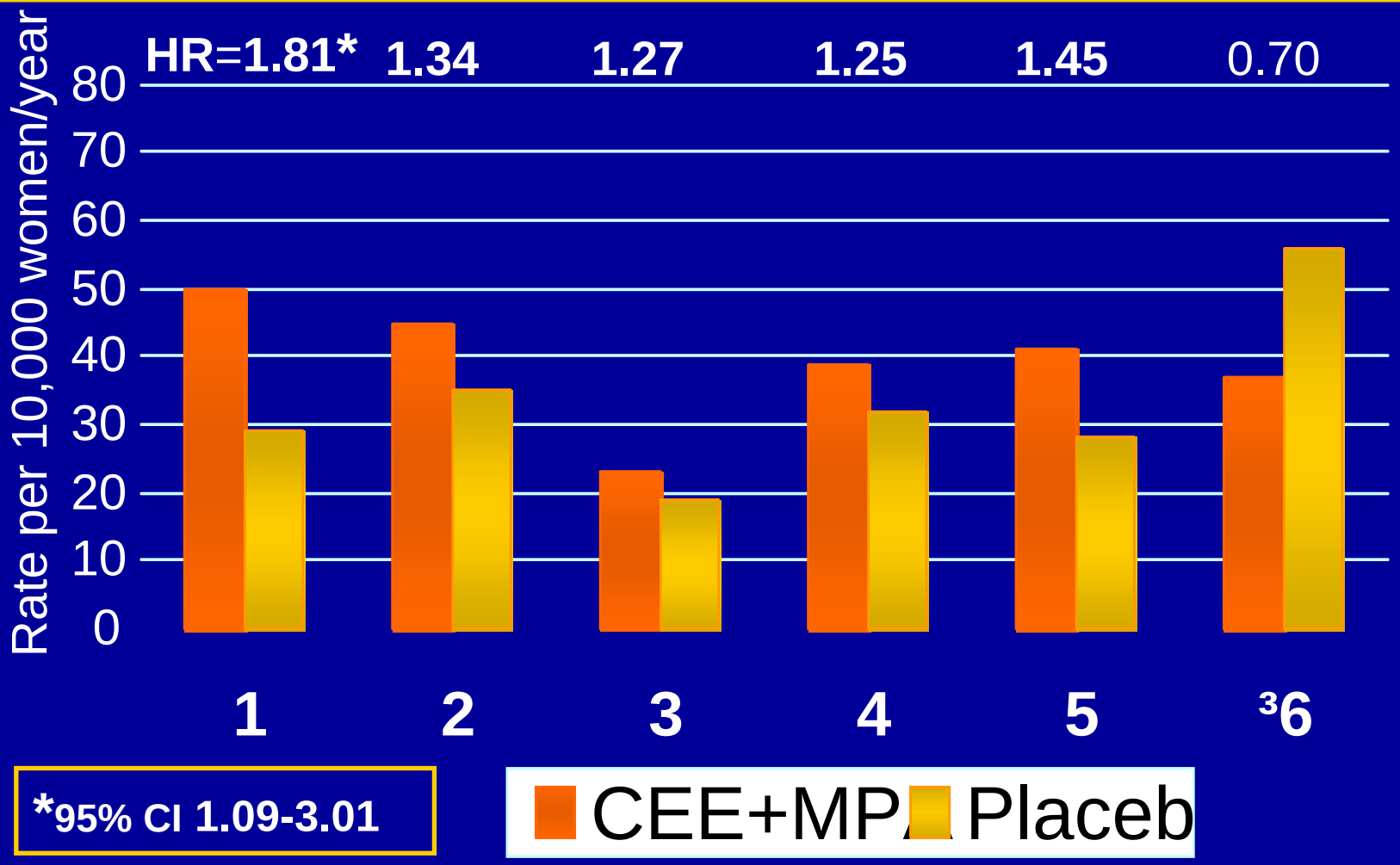
**Preliminary Findings*



***Statistically significant based on 95% nominal CI on Hazard Ratios**

Adapted from: Writing Group for the Women's Health Initiative. **JAMA. 2002;288:321-333**

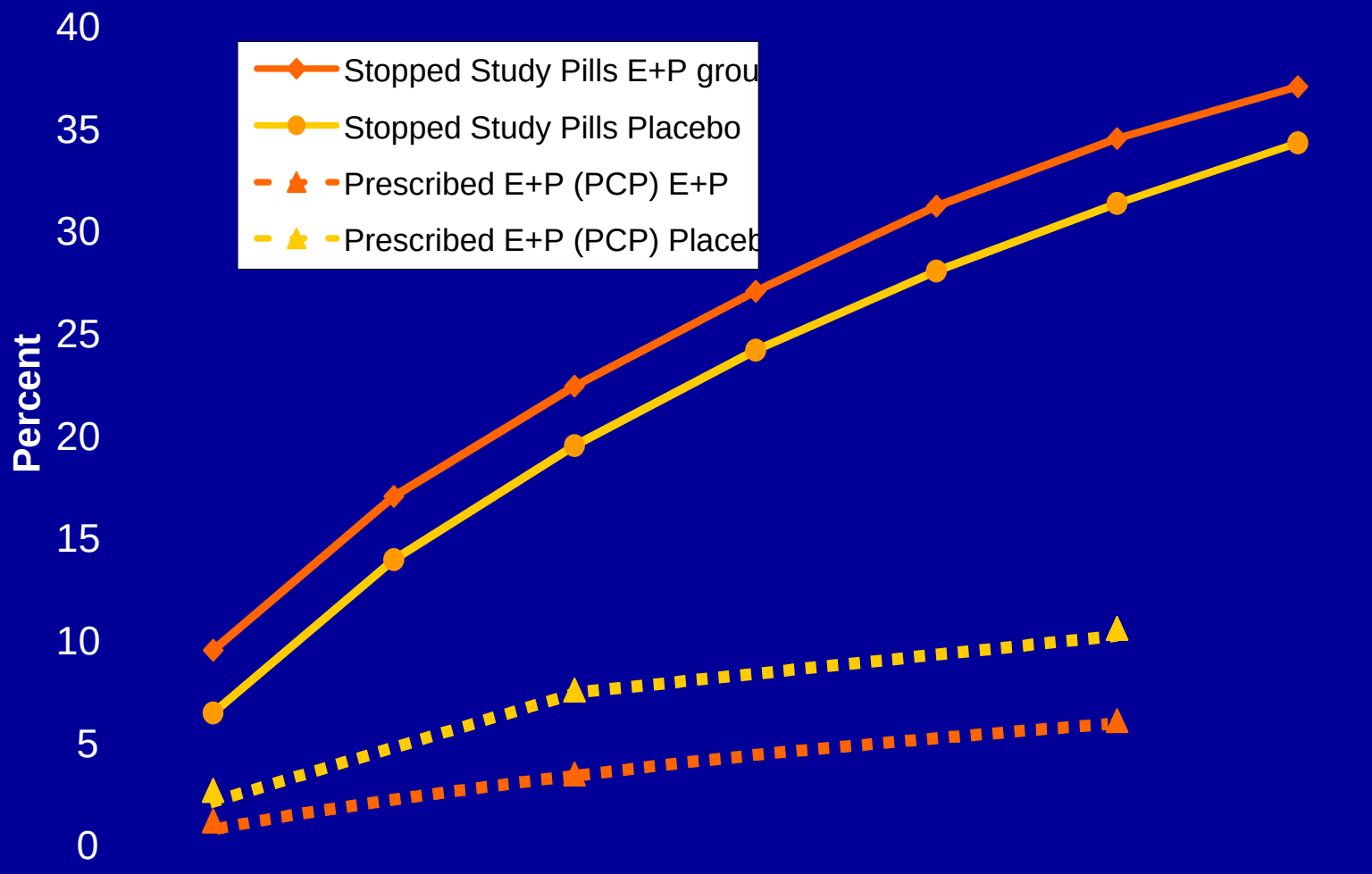
WHI E+P: CHD Rates per 10,000/year Year of Follow-Up



*95% CI 1.09-3.01

Manson et al, **NEJM 2003; 249: 523-534**

WHI E+P: Cumulative Discontinuation and "Drop-in" Rates by Randomization Assignment and Follow-up Time



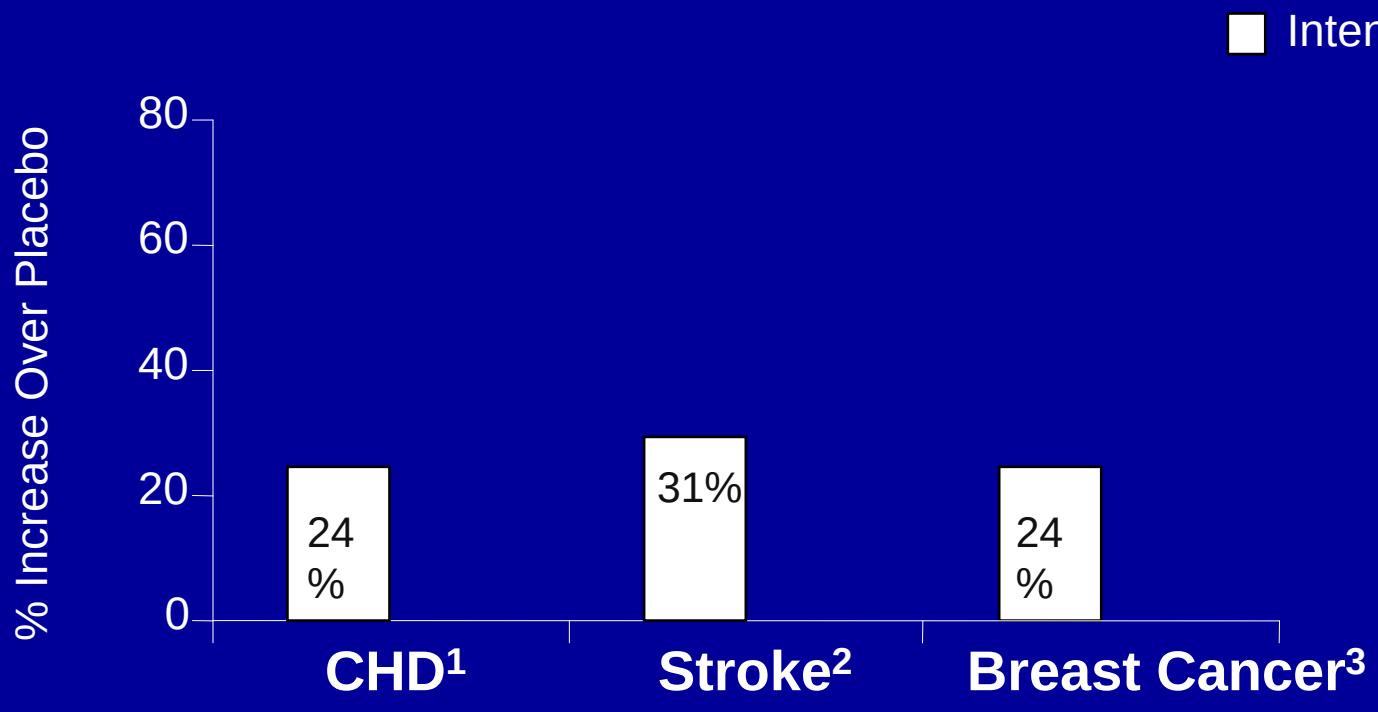
Writing Group for WHI Investigators: **JAMA 2002; 288: 321-333**

WOMEN'S HEALTH INITIATIVE

WHI E+P Trial: Primary Endpoints

Percent Event Rates Based on Analysis Type

Final centrally-adjudicated outcomes - 2003 (average 5.6 yrs of follow-up)



1 Manson JE et al **N Engl J Med 2003; 349: 523-534**

2 Wassertheil-Smoller S et al **JAMA 2003; 289: 2673-2684**

3 Chlebowski RT et al. **JAMA 2003; 289: 3243-3253**

WOMEN'S HEALTH INITIATIVE

WHI E+P Trial: Primary Endpoints

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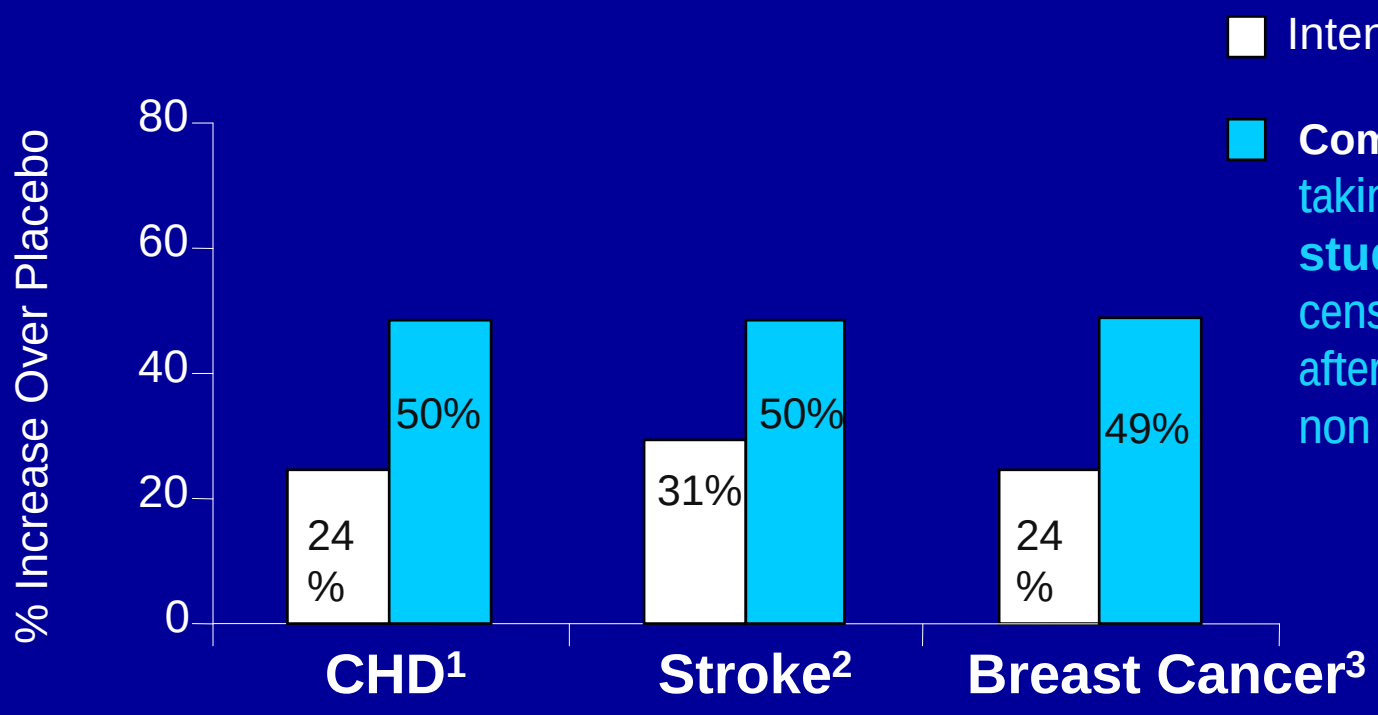


1 Manson JE et al **N Engl J Med 2003; 349: 523-534** **HR: 1.50 (1.14-1.97)**

2 Wassertheil-Smoller S et al **JAMA 2003; 289: 2673-2684** **HR: 1.50 (1.08-2.08)**

3 Chlebowski RT et al. **JAMA 2003; 289: 3243-3253** **HR: 1.49 (1.13-1.96)**

WOMEN'S HEALTH INITIATIVE

WHI Memory Study (WHIMS) - ancillary study

(Postmenopausal Women, aged 65-79)

WHIMS E+P and E-only trials = 7,479

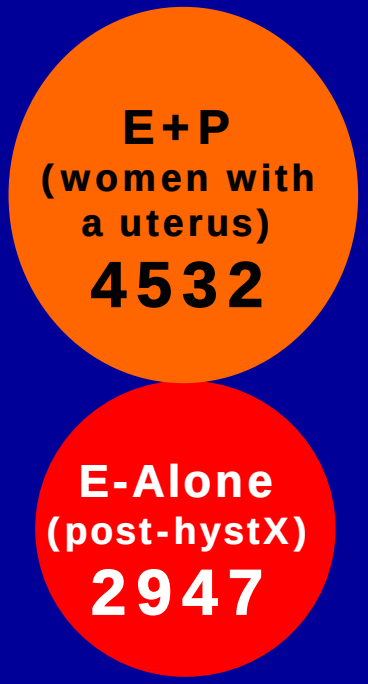
Primary Outcome:

- Probable Dementia (PD)

Secondary Outcomes:

- Combined PD & Mild Cognitive Impairment (MCI)

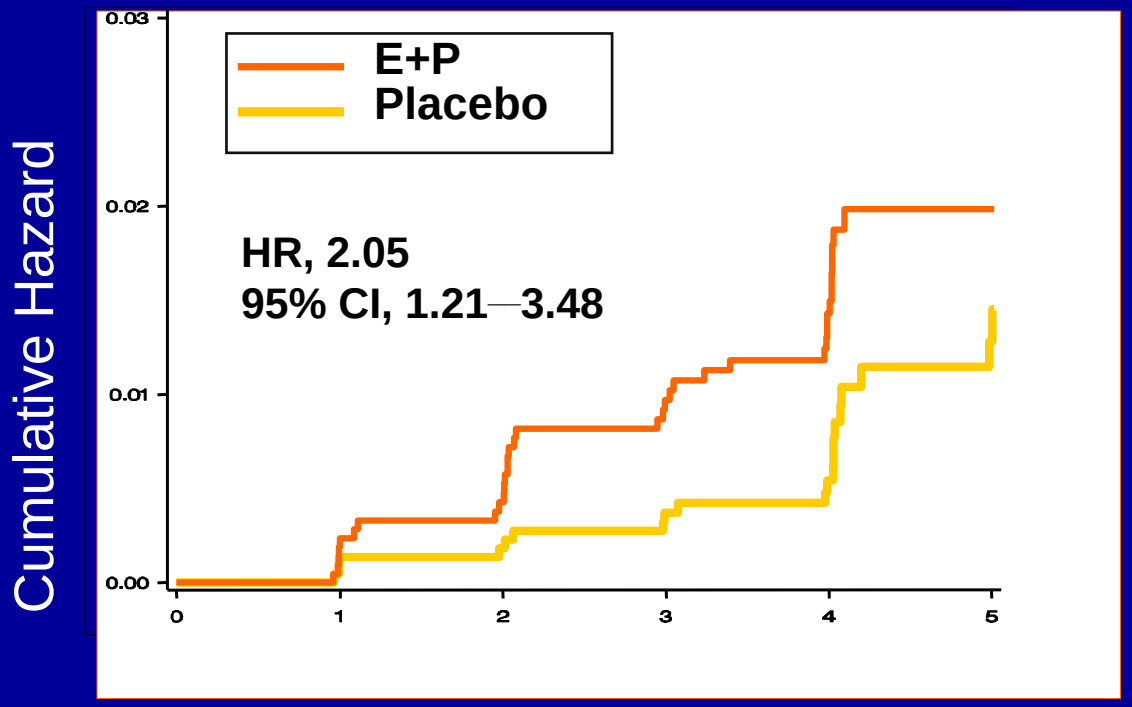
- Supporting Data:
  Global Cognitive Function
  (by annual Modified Mini-mental State Examination, 3MSE))



*design ~ 7 years

WHIMS E+P: Probable Dementia Hazard Ratio

4532 women, aged 65-79; followed for 4.1 years



No. at Risk

E+P	2229	2112	2026	1915	1325	401
Placebo	2303	2200	2125	1984	1392	477

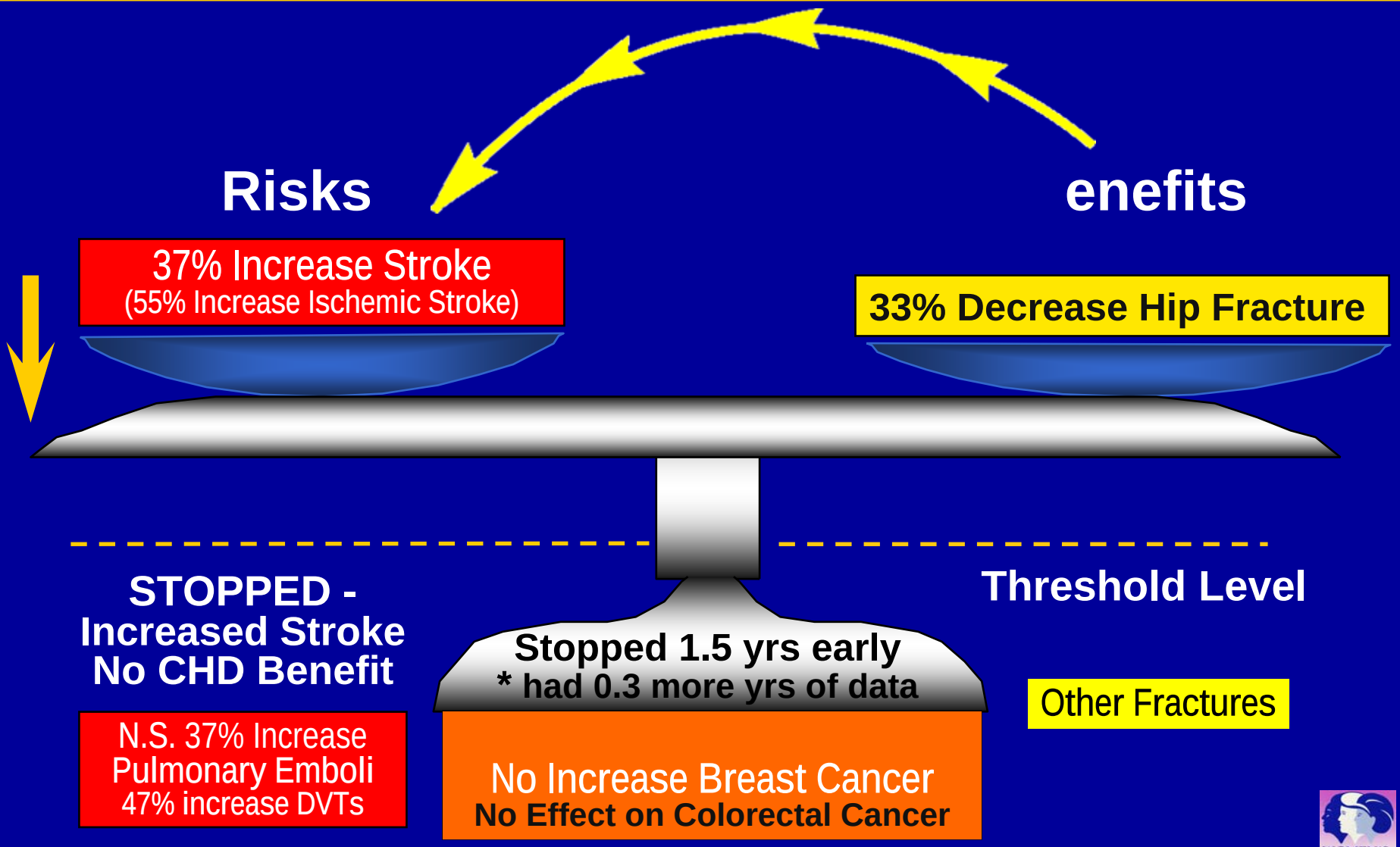
Key Randomized Clinical Trials of Menopausal Hormones

- **1995** - **PEPI** (CEE ± 3 Progestin arms, for CHD risk) published (JAMA)
- **1998** - **HERS** (CEE+MPA in women with CHD) published (JAMA)
- **2002** - **WHI E+P** (CEE+MPA): risks outweigh benefits (JAMA)
- **2003 - FDA: "black box" warning on estrogen products:**

> **Estrogens and progestins should not be used for the prevention of cardiovascular disease.**
>
> **…..estrogens** with or without progestins **should be prescribed at lowest effective doses and for the shortest duration consistent with treatment goals and risks for individual woman.**

- **2004** - **WHI E-Alone** (CEE): no CHD benefit, risks=benefits (JAMA)

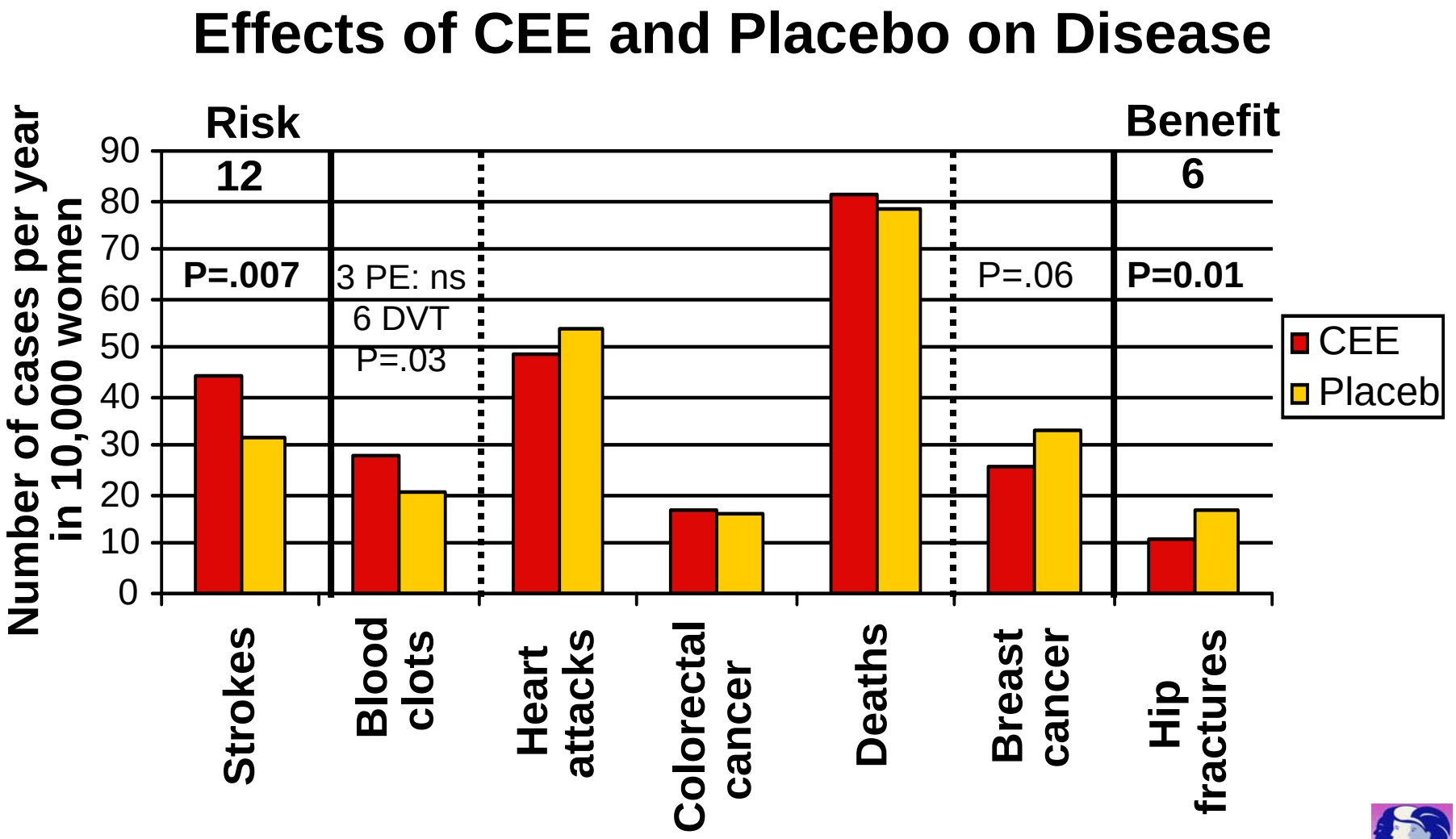
WHI E only Trial: Preliminary Findings, March 2004 (aver. 6.8 yrs)



*Adapted from: Writing Group for the Women's Health Initiative. **JAMA. 2002;288:321-333**

WHI E-Alone (CEE) Trial: Absolute (annualized) Risk (6.8 Yrs*)

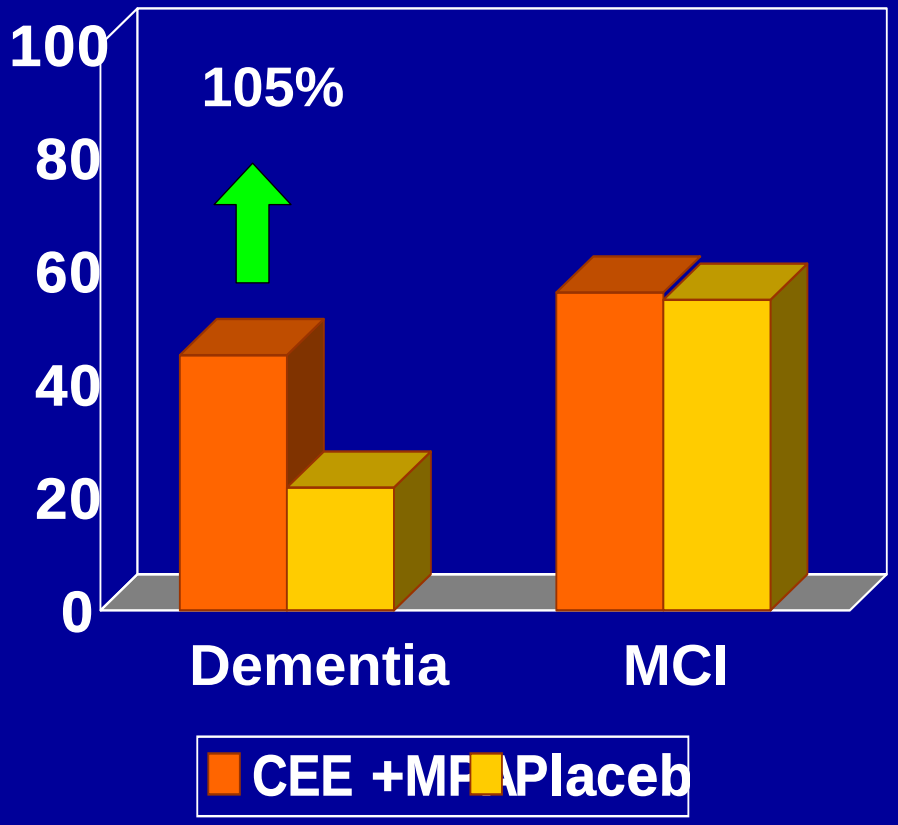
Preliminary Findings



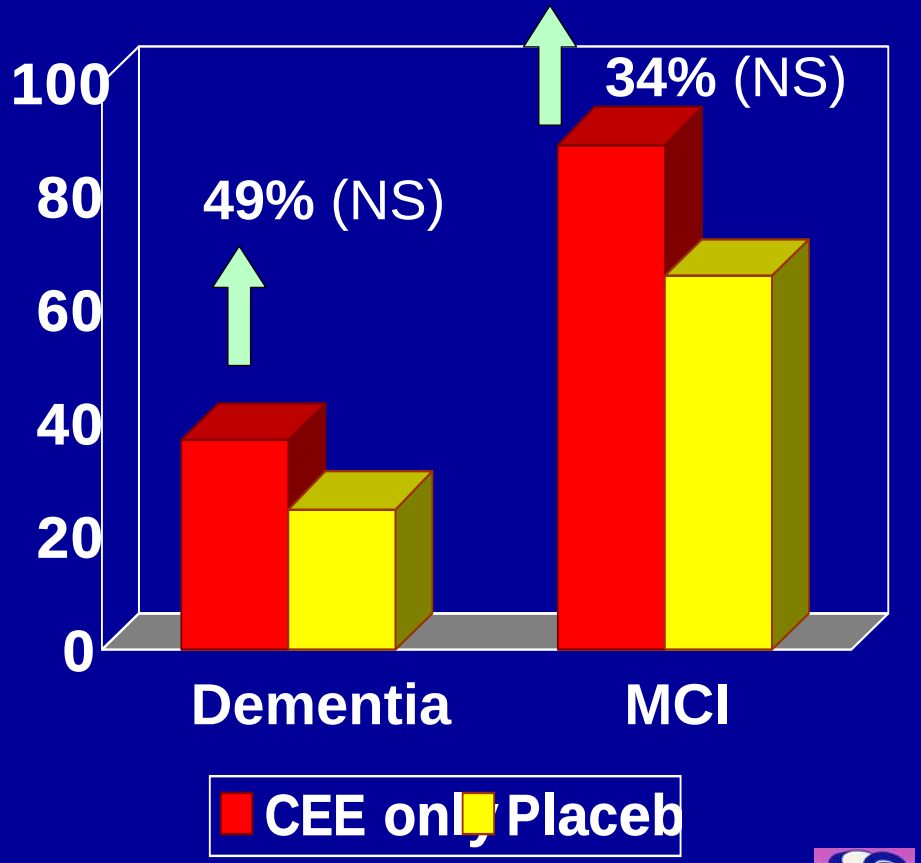
WHIMS (Women aged ≥ 65 years): Rates per 10,000/year

Probable Dementia & Mild Cognitive Impairment

N=**4,532**; **4.1 yrs** follow-up



N=**2,947; 5.2 yrs** follow-up



JAMA 2003; 289:2651-2662

2958

WOMEN'S HEALTH INITIATIVE

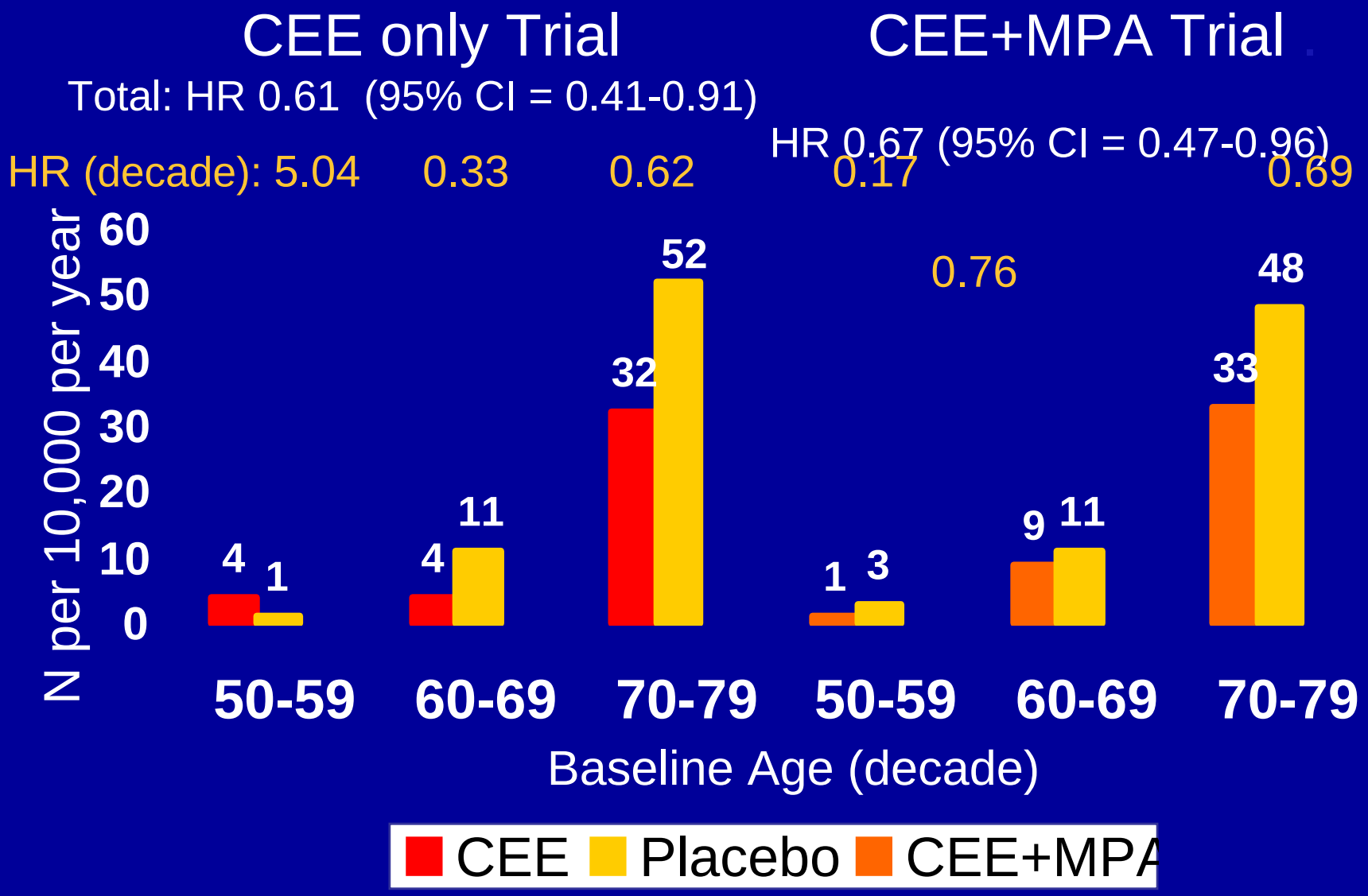
Summary: WHI E+P* vs. E-Alone** Trial

*published: *July 2002 **April 2004*

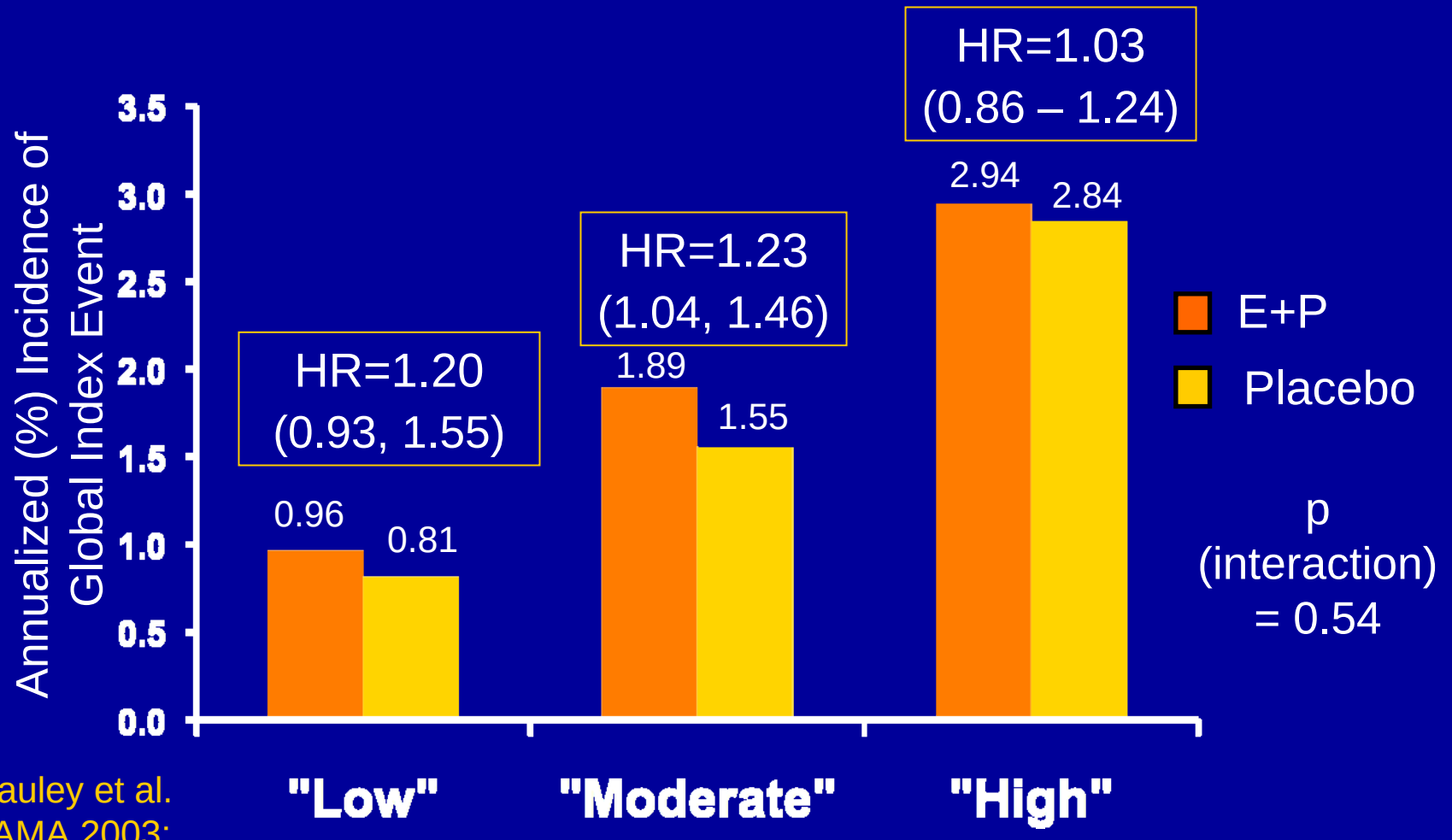
- **Concordant results**
  - **Heart Disease – no benefit *(for E+P, early harm)***
  - **Strokes, Blood Clots – harmful**
  - **Fractures – beneficial**
  - **Dementia (if ≥ 65 yrs of age) – harmful**
- **Disparate Results**
  - **Breast Cancer**
    - **Increased in E+P Trial** (women with a uterus)
    - **Not increased in E-Alone Trial** (women with prior hysterectomy)
      - Increased breast cancer risk in women with highest baseline risk
  - **Global Index**
    - **Increased in E+P (CEE + MPA) Trial**
    - **Neutral in E-Alone (CEE) Trial**

WOMEN'S HEALTH INITIATIVE

WHI Hip Fracture by Age: Annualized Rates, Hazard Ratios



WHI E+P Trial: Effects of CEE+MPA on the Global Index by Fracture Risk Score

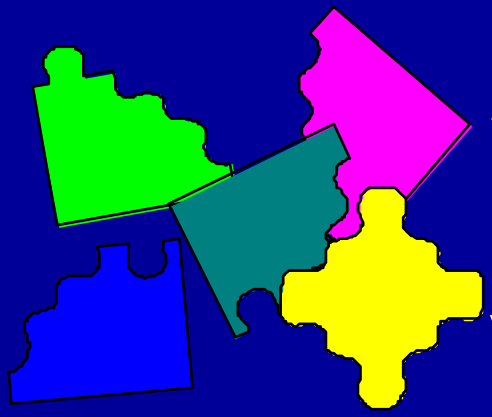


Cauley et al. JAMA 2003; 290: 1729-1738

HT Puzzle: Individualize Benefit to Risk Ratio

Estrogens reduce peri-**menopausal symptoms, e.g. hot flushes**

Postmenopausal Hormone Therapy (Aging):



Heart Disease - No Benefit (E+P, early harm)

NOT for CHD Prevention (FDA)

Stroke - increases risk

Blood Clots (Lungs, Legs) - increases risk

Hip Fractures - reduces risk

Vertebral Fractures - definitely favorable

Breast Cancer - E+P increases risk

Estrogen only - no increase by 7.1 years

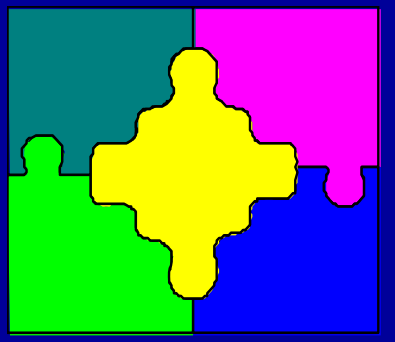
[Increased in women with highest baseline risk]

Dementia, MCI - increases risk

[in women ≥65 yrs of age]

Gallbladder Disease - increases risk

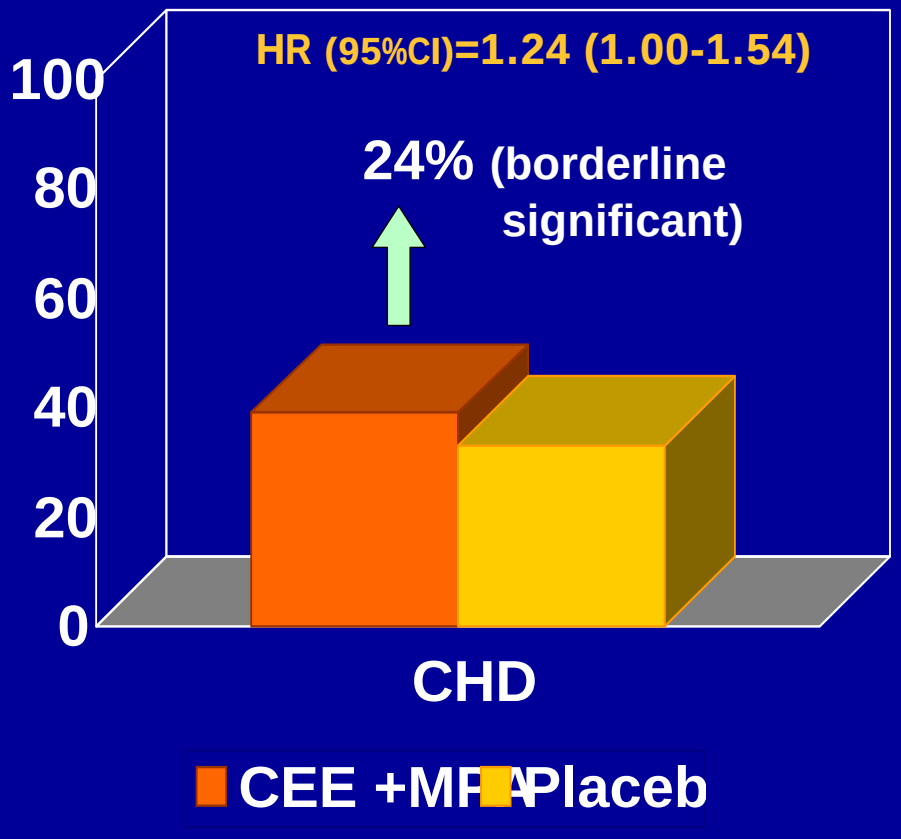
Incontinence - increases risk



WHI HT: (Women aged 50-79 years): Rates per 10,000/year

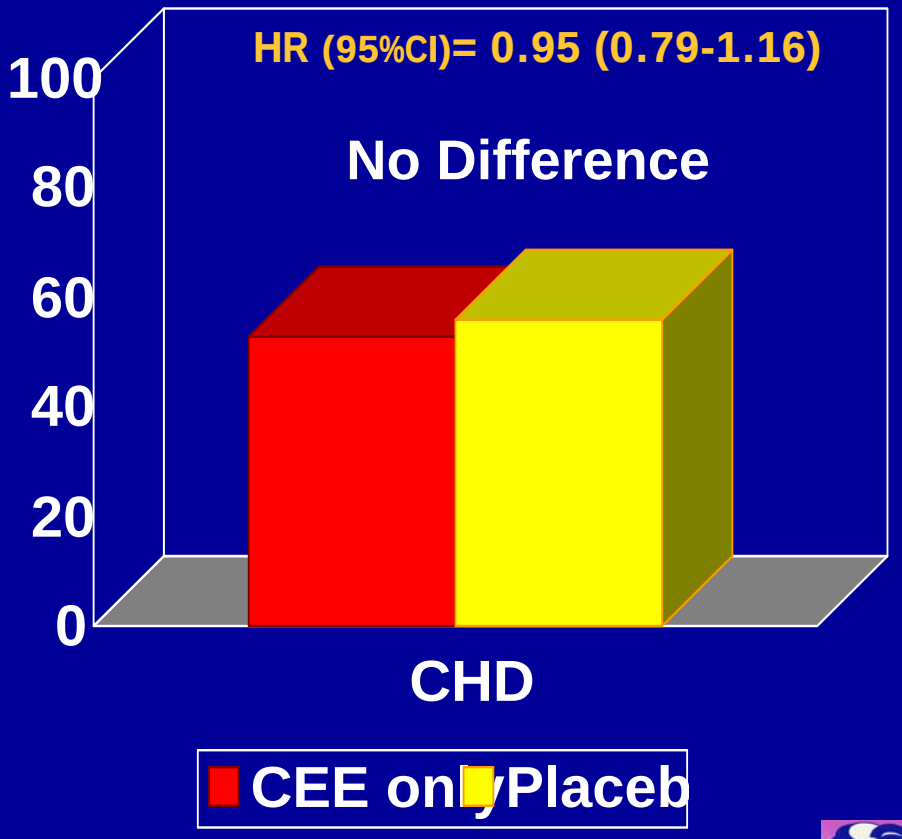
CORONARY HEART DISEASE

N=**16,608**; **5.6 yrs** follow-up



N Engl J Med 2003: 349; 523-534

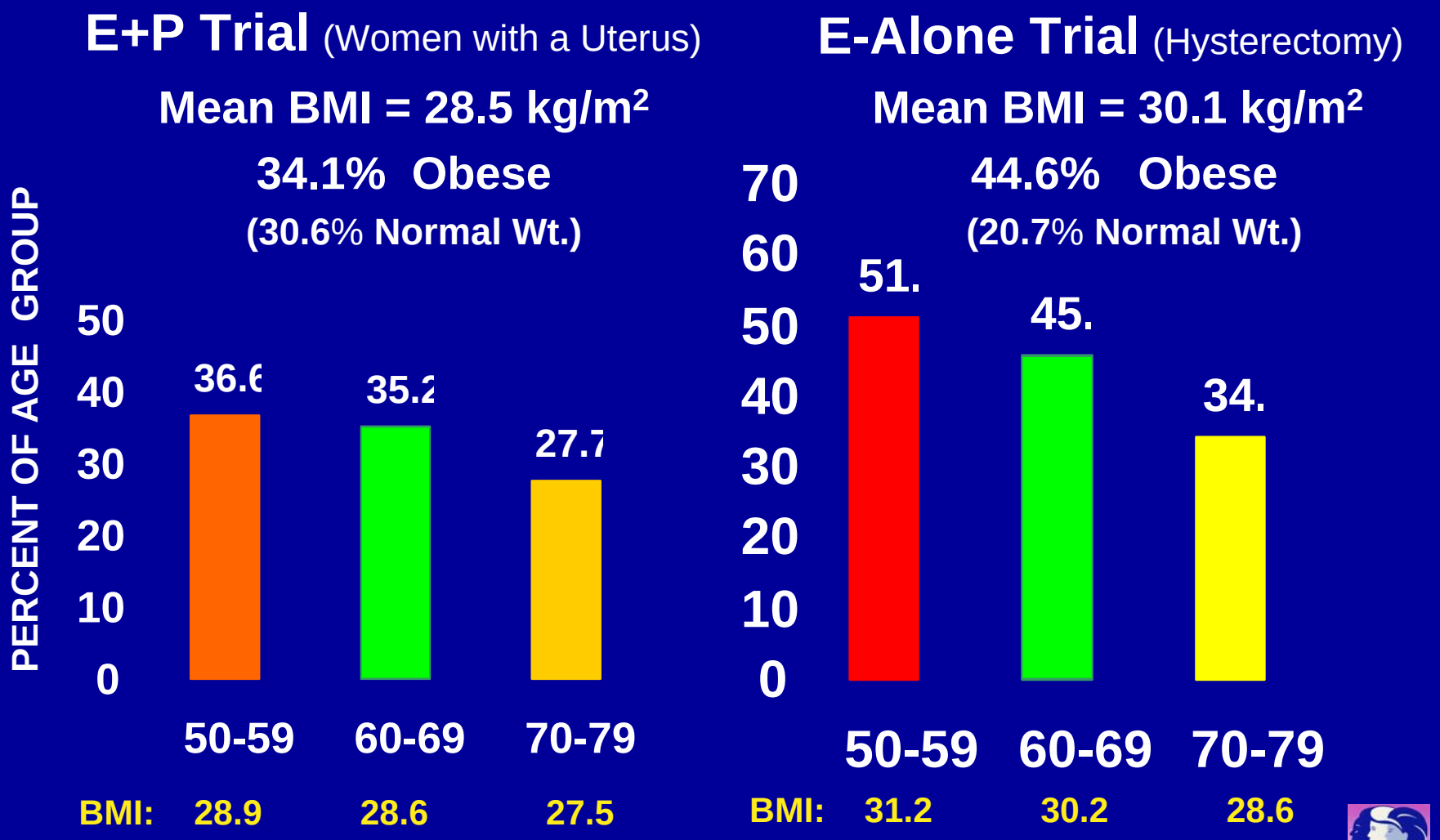
N=**10,739; 7.1 yrs** follow-up



Arch Intern Med 2006; 166:357-36

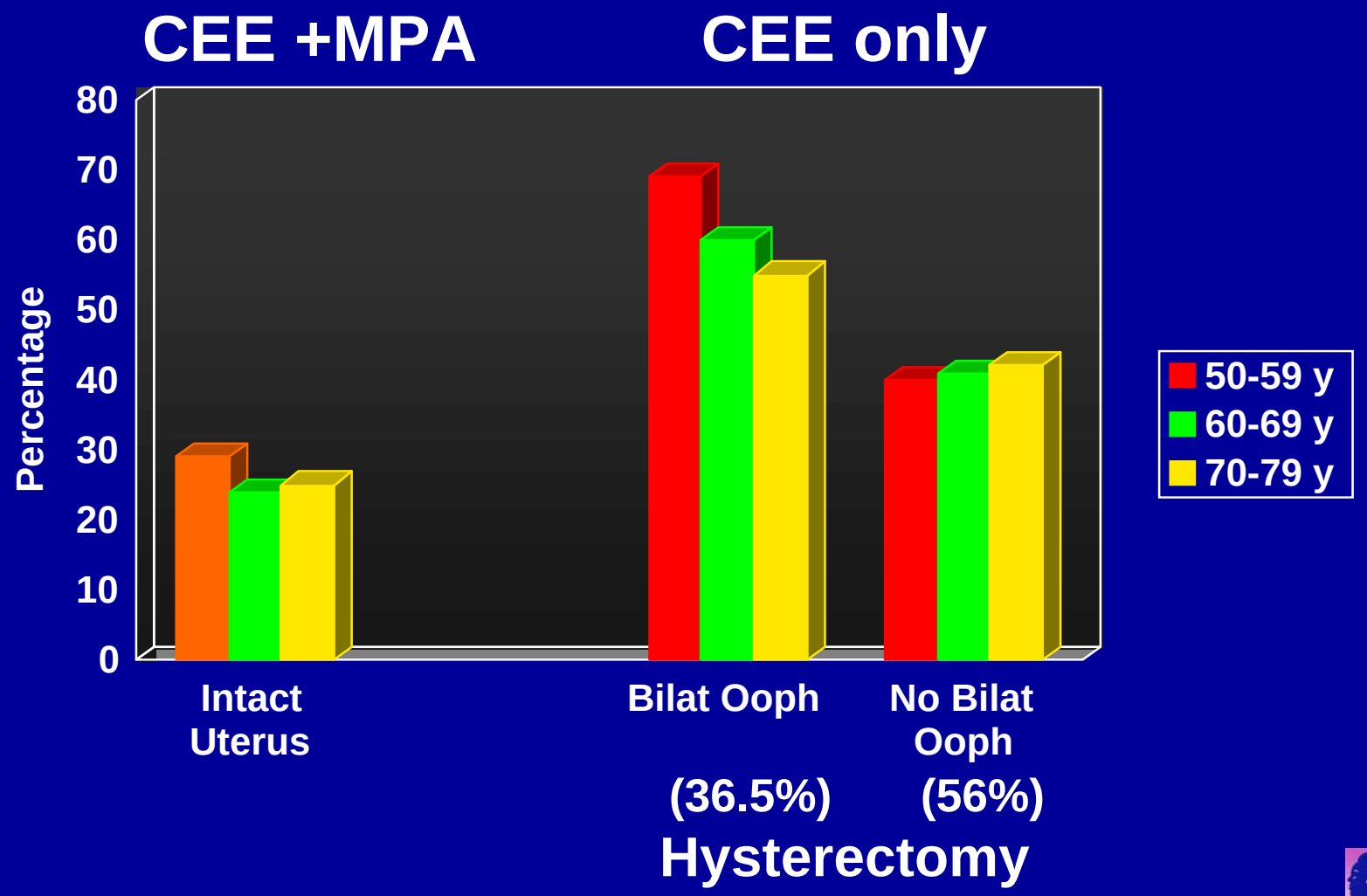
WOMEN'S HEALTH INITIATIVE

WHI Hormone Trials: Percent Obese (BMI ≥30 kg/m²)



Stefanick, et al Ann Epidemiol 2003; 13: S78-S86

Prior HT Use by Age at Baseline



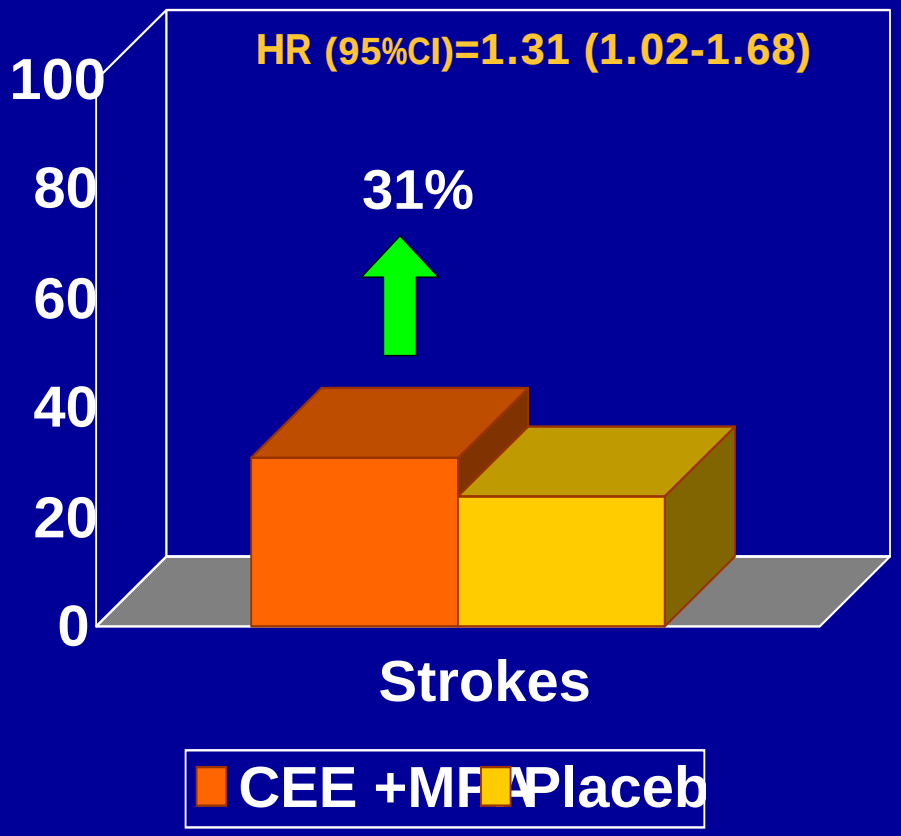
Rossouw JAMA 2007;297:1465-1477

WOMEN'S HEALTH INITIATIVE

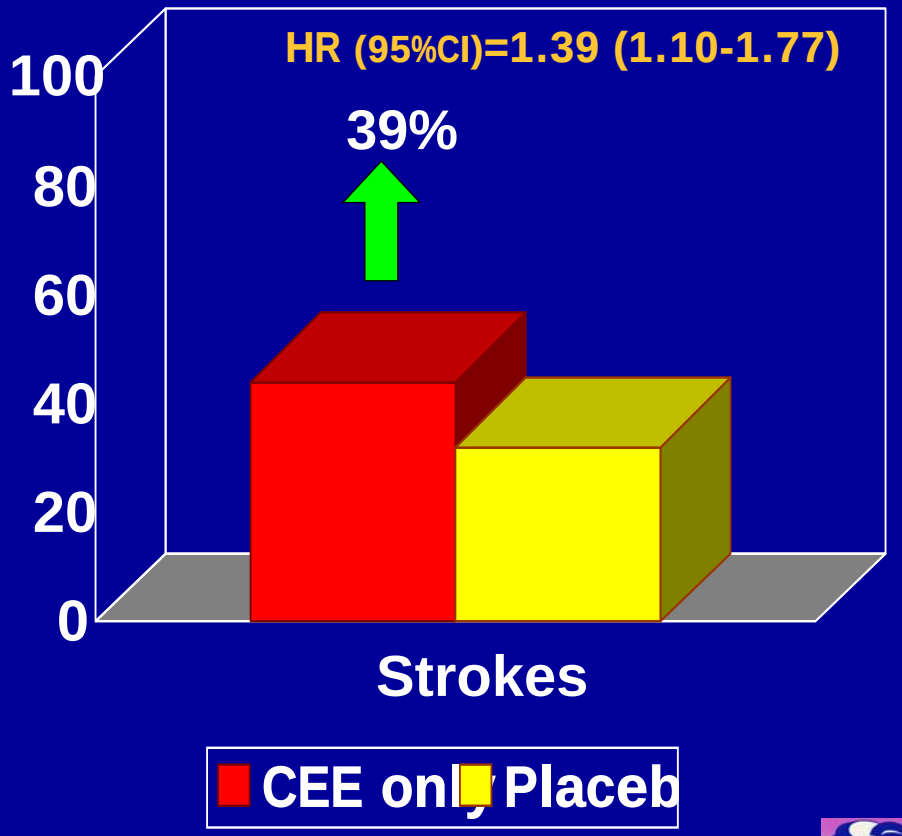
WHI (Women aged 50-79 years): Rates per 10,000/year

STROKES

N=**16,608**; **5.6 yrs** follow-up



N=**10,739; 6.8 yrs** follow-up



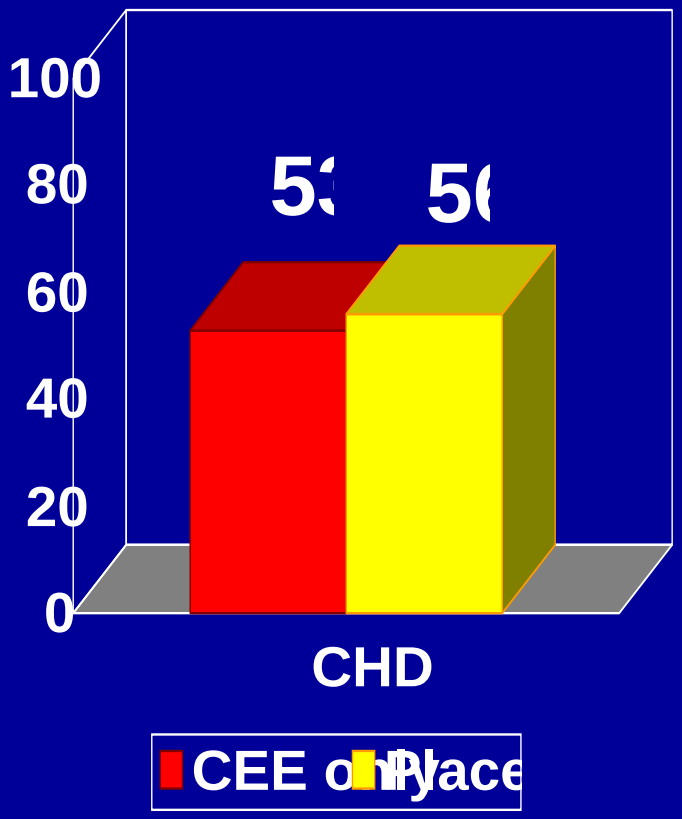
JAMA 2003; 289: 2673-2684

WOMEN'S HEALTH INITIATIVE

WHI E-alone: CORONARY HEART DISEASE (CHD) Total and by Age (Rates per 10,000/year)

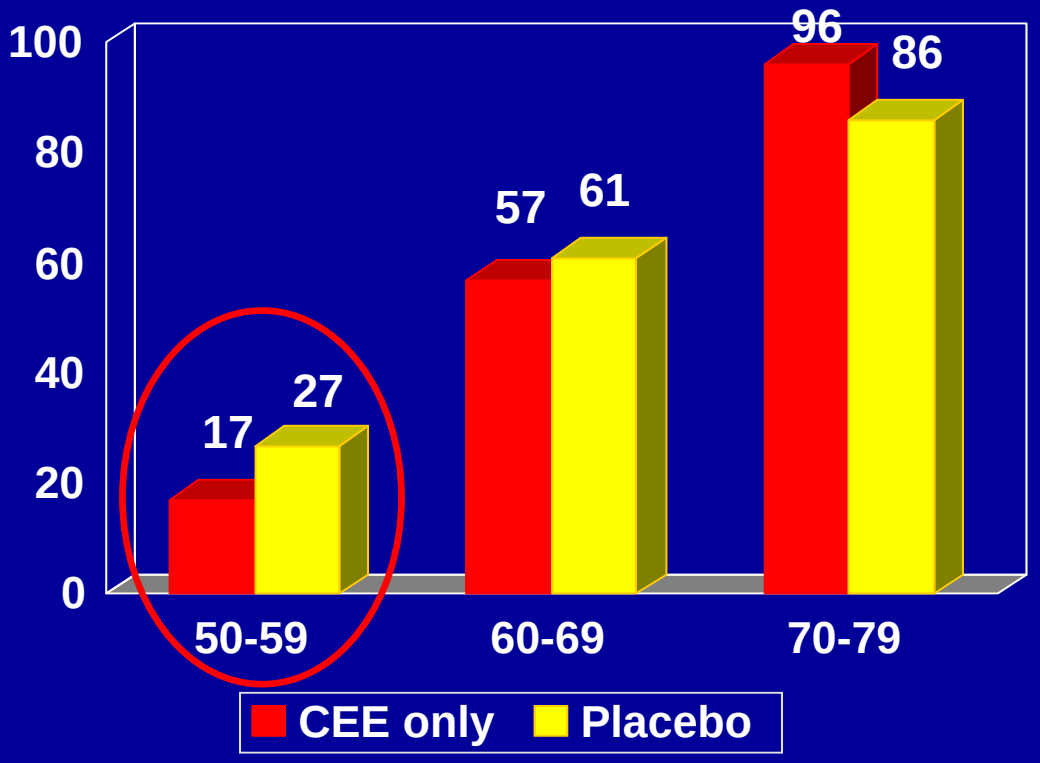
N=**10,739; 7.1 yrs** follow-up

HR= **0.95 (95%CI: 0.79-1.16)**



p = 0.07 for interaction

50-59	60-69	70-79
HR: 0.63 (0.36-1.08)	**HR: 0.94** (0.71-1.24)	**1.11** (0.82-1.52)



Hsia et al **Arch Intern Med 2006; 166:357-365.**

WHI Estrogen Only: Coronary Events (HR, 95% CI) with CEE or Placebo by Age at Enrollment

	50-59	60-69	70-79	P for Interaction
CHD (MI or coronary death)	0.63 (0.36-1.08)	0.94 (0.71-1.24)	1.11 (0.82-1.52)	0.07
CABG/Percutaneous Coronary Intervention	0.55 (0.35-0.86)	0.99 (0.78-1.27)	1.04 (0.78-1.39)	0.09
Confirmed Angina (Hosp., stress test or Obstr. CD by angiogr.)	0.59 (0.34-1.02)	1.03 (0.76-1.41)	1.12 (0.78-1.60)	0.18
All of the above combined	0.66 (0.45-0.96)	0.98 (0.80-1.20)	1.05 (0.84-1.33)	0.11

Hsia et al **Arch Intern Med 2006; 166:357-365.**

WOMEN'S HEALTH INITIATIVE

Secondary analyses of Combined WHI Trials
Numbers of Participants

Age			Years Since Menopause		
	N	%		N	%
50-59	8,832	32.3%	<10	7,137	29.4%
60-69	12,362	45.2%	10-19	8,977	36.9%
70-79	6,153	22.5%	≥20	8,203	33.7%
Total	27,347	100%	Total	24,317*	100%

* 3,030 missing values

Rossouw et al **JAMA 2007;297:1465-1477**

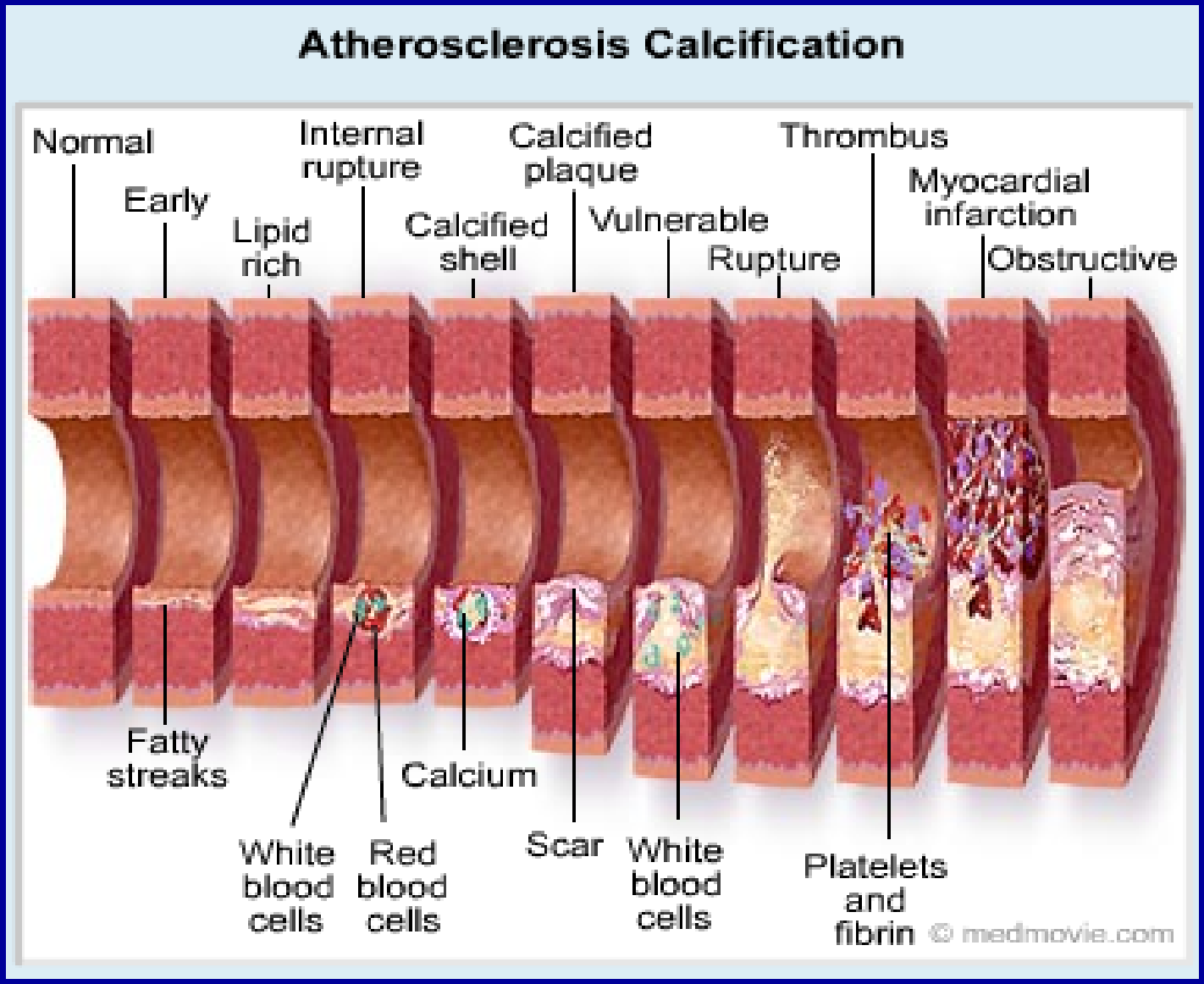
WOMEN'S HEALTH INITIATIVE

Principal findings from secondary analyses of Combined WHI Trials (2007)

- **Women starting hormones close to the menopause may have fewer heart attacks and deaths due to HT compared to increases in women distant from the menopause**
- **Provides some reassurance that younger women using hormones for the short term for relief of hot flashes and night sweats are not at increased risk of heart disease**
- **Stroke increased irrespective of age or years since menopause (*Breast cancer also increased in E+P only)***
- **Older women with moderate/severe hot flashes or night sweats appear to be at high risk if they start hormone therapy**
  - In part explained by **higher prevalence of risk factors** (obesity, high blood pressure, high blood cholesterol, diabetes) **in women with vasomotor symptoms**

Rossouw et al **JAMA 2007;297:1465-1477**

WOMEN'S HEALTH INITIATIVE


Atherosclerosis Calcification
Normal
Early
Lipid rich
Internal rupture
Calcified shell
Calcified plaque
Vulnerable
Rupture
Thrombus
Myocardial infarction
Obstructive
Fatty streaks
White blood cells
Red blood cells
Calcium
Scar
White blood cells
Platelets and fibrin
© medmovie.com

WHI Coronary Artery Calcium Study (CACS)

- **Women aged 50-59 at time of randomization into E-Alone trial (with prior hysterectomy) at 28 (of 40) WHI sites**
- **After mean 7.4 years of treatment; 1.3 yrs after trial was completed**

  - Did not study older women in E-only trial or women in E+P trial

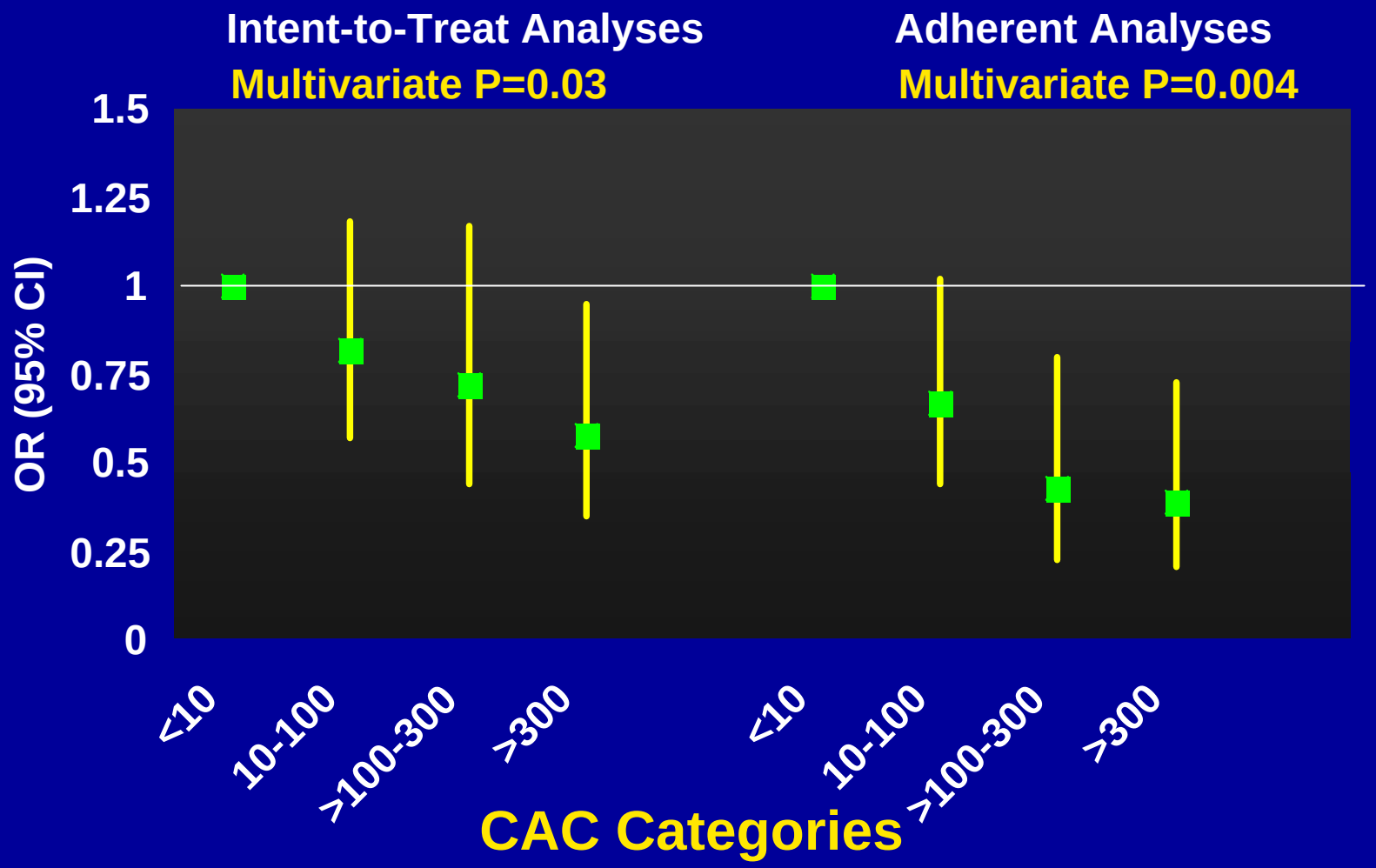
Baseline Characteristics (N=1064: 537 CEE, 527 Placebo)

- **Age: Mean 55 (50-54, 39.5%; 55-59, 60.5%)**
- **Age at Menopause: Mean 43.5**
- **Age at Hysterectomy: < 35 (28%); 35-39 (25%); 40-44 (22.5%); ≥ 45 (23%)**
- **Ethnicity: White, ~ 75% Black, 16.5% Hispanic, 6% Asian/PI, 0.3%**
  American Indian, <1%
- **Body Mass Index: 30.5 kg/m²; Hypertension: 35.5%; Diabetes: 6.3%**

Manson et al, **NEJM 2007; 356: 2591-2602**

WOMEN'S HEALTH INITIATIVE

Odds Ratios for Various Categories of Elevation in Coronary Artery Calcium (CAC) Score in 1064 Women Aged 50-59 in WHI CEE Trial



Manson et al, **NEJM 2007; 356: 2591-2602**

Summary & Conclusions

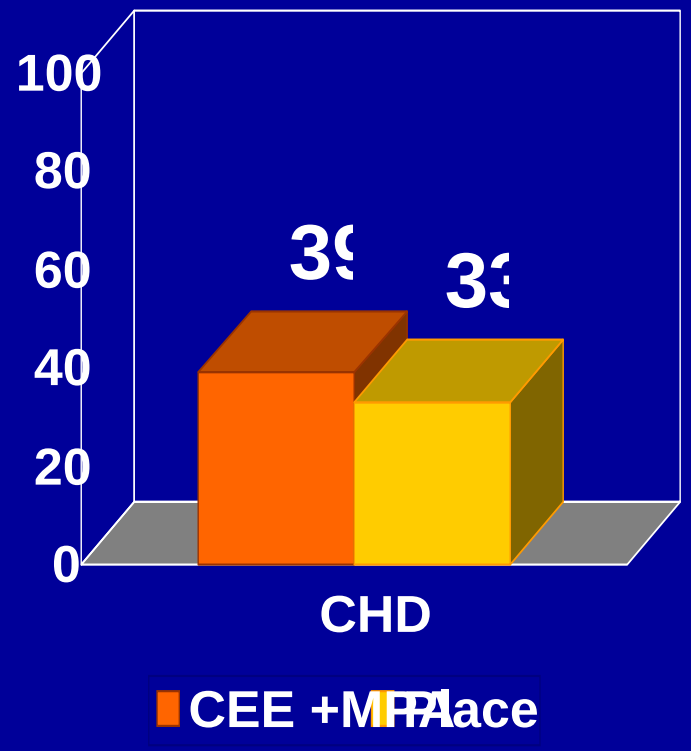
- **Among women aged 50-59 in E-alone Trial calcified plaque burden in coronary arteries was lower in CEE group than placebo 1.3 yrs after 7.4 yrs of treatment. Did not study older women or E+P trial**
- **WHI data do not suggest CHD harm for short-term therapy to relieve menopausal symptoms.**
- **N Engl J Med Editorial *entitled:* HRT and the Young at Heart**
  - **Mendelsohn ME, Karas RH. NEJM 2007; 356: 2639-2641**
  - **Timing Hypothesis: The beneficial effects of "HRT" in preventing atherosclerosis occur only when the therapy is initiated before advanced atherosclerosis develops.**
    - **Predicts that HRT is NOT beneficial when given to older women, because the underlying biologic characteristics of the vessel wall and vascular response to HRT are altered in older, more atherosclerotic vessels.**
- **Age is a powerful risk factor** for atherosclerosis; **risk is low for majority of women aged 50-59.**

WOMEN'S HEALTH INITIATIVE

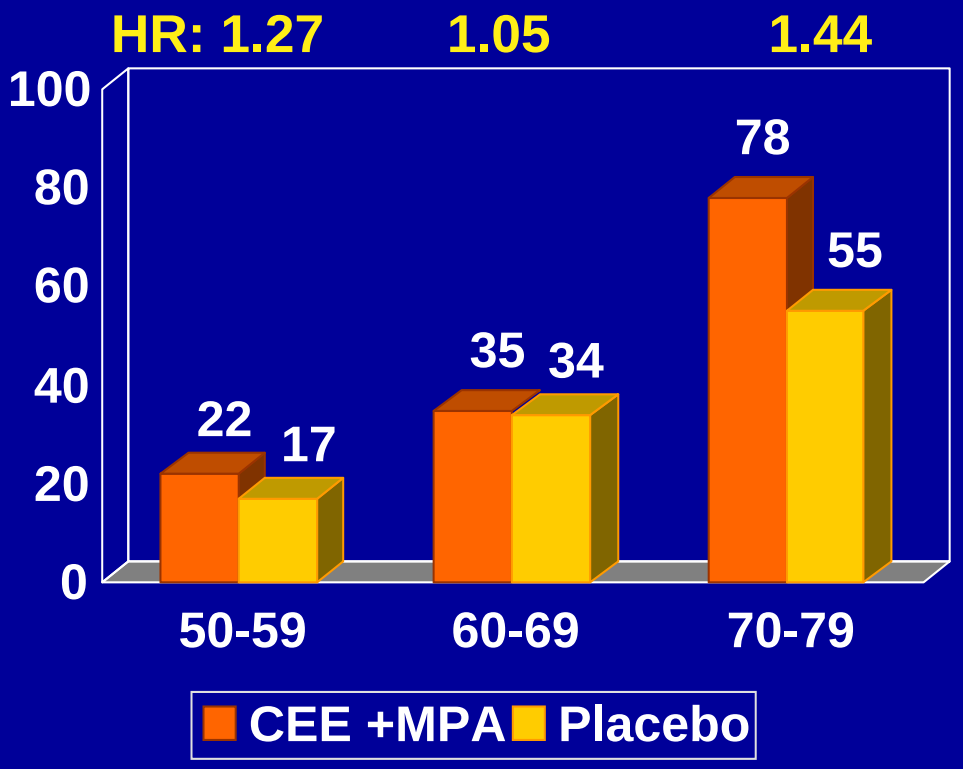
WHI E+P: CORONARY HEART DISEASE (CHD)
Total and by Age (Rates per 10,000/year)

N=**16,608**; 5**.6 yrs** follow-up*

HR =1.24 (95%CI,**1.00-1.54)**



p= 0.36 for interaction



*Yr 1: HR =**1.81** (95% CI, **1.09-3.01)**

Manson et al, **NEJM 2003; 249: 523-534**

WOMEN'S HEALTH INITIATIVE

WHI E+P: Post-Intervention Follow-up

After E+P trial was stopped early, WHI followed study participants through the planned termination of the trial *(March 31, 2005)*

Except for stopping the intervention and unmasking, the same trial protocol was followed, e.g. semi-annual monitoring to identify and classify study outcomes

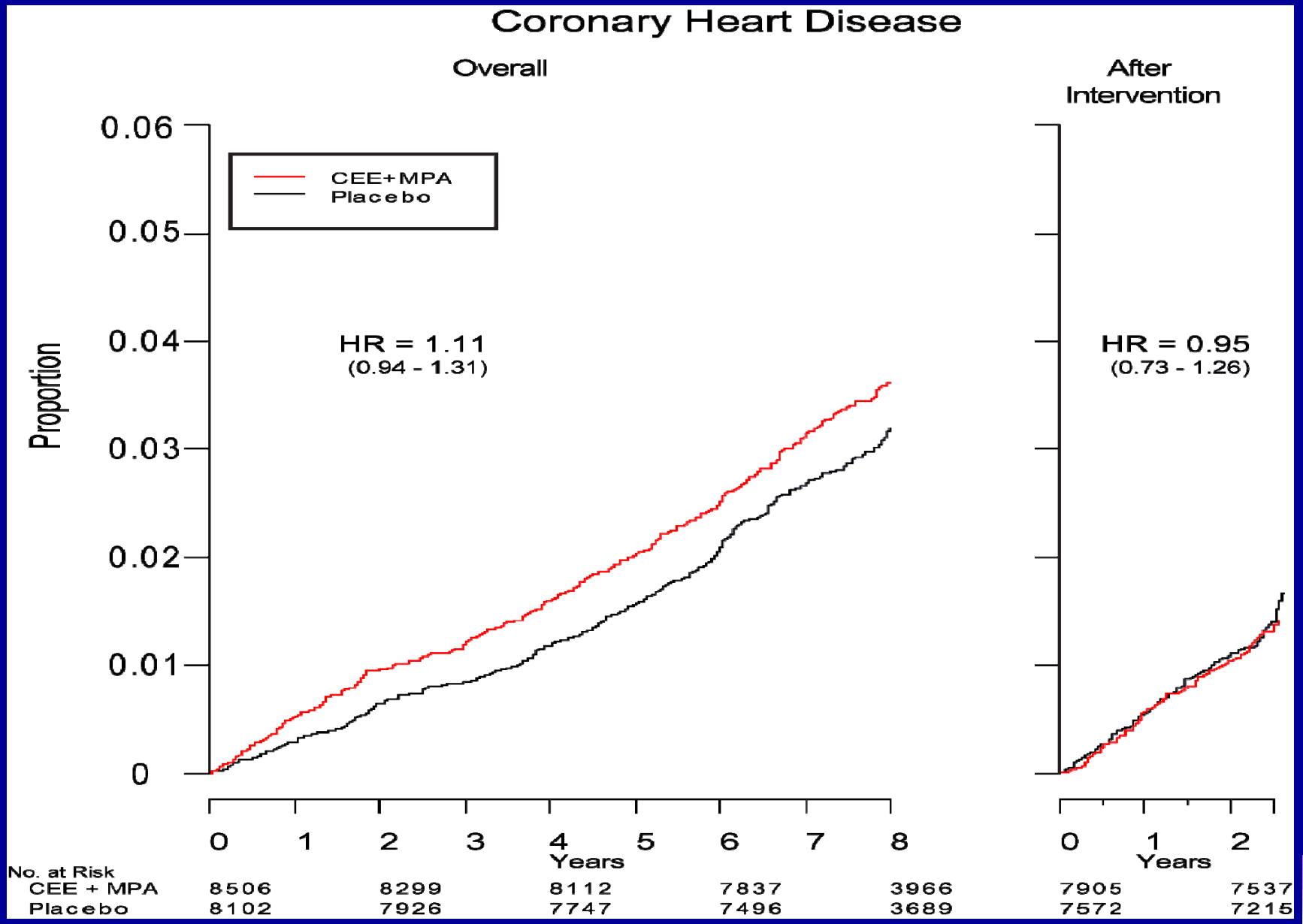
Post-intervention information *(for July 8, 2002 to March 31, 2005)* was available on 95% of the women: mean of 2.4 years of follow-up

***WHI is continuing to follow the participants and plans to publish after 3 more years of follow-up in the future*.**

WHI E-Alone trial follow-up data will be published next year.

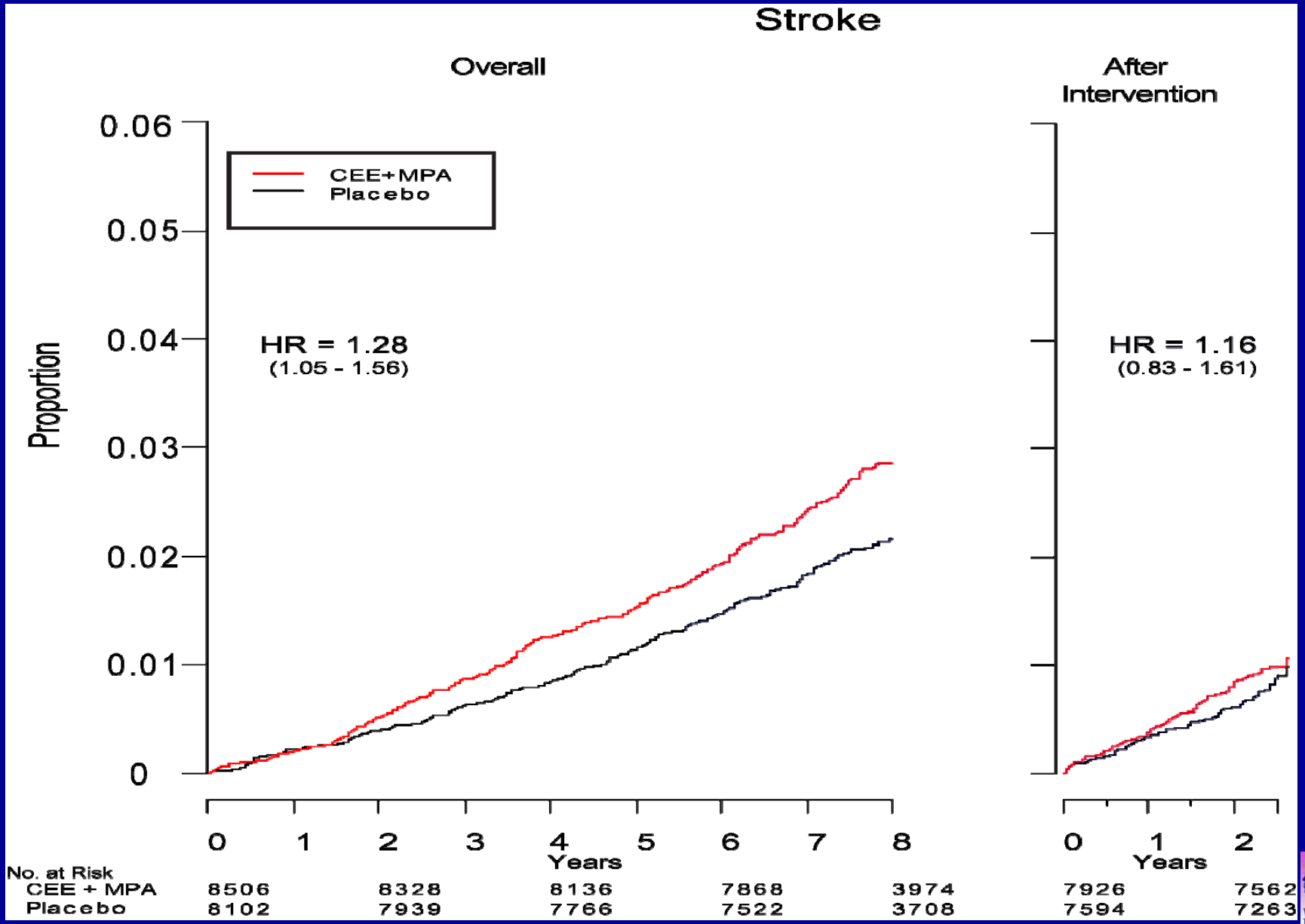
Heiss et al, **JAMA 2008; 299: 1036-1045**

WHI E+P: Post-Intervention Follow-up CHD



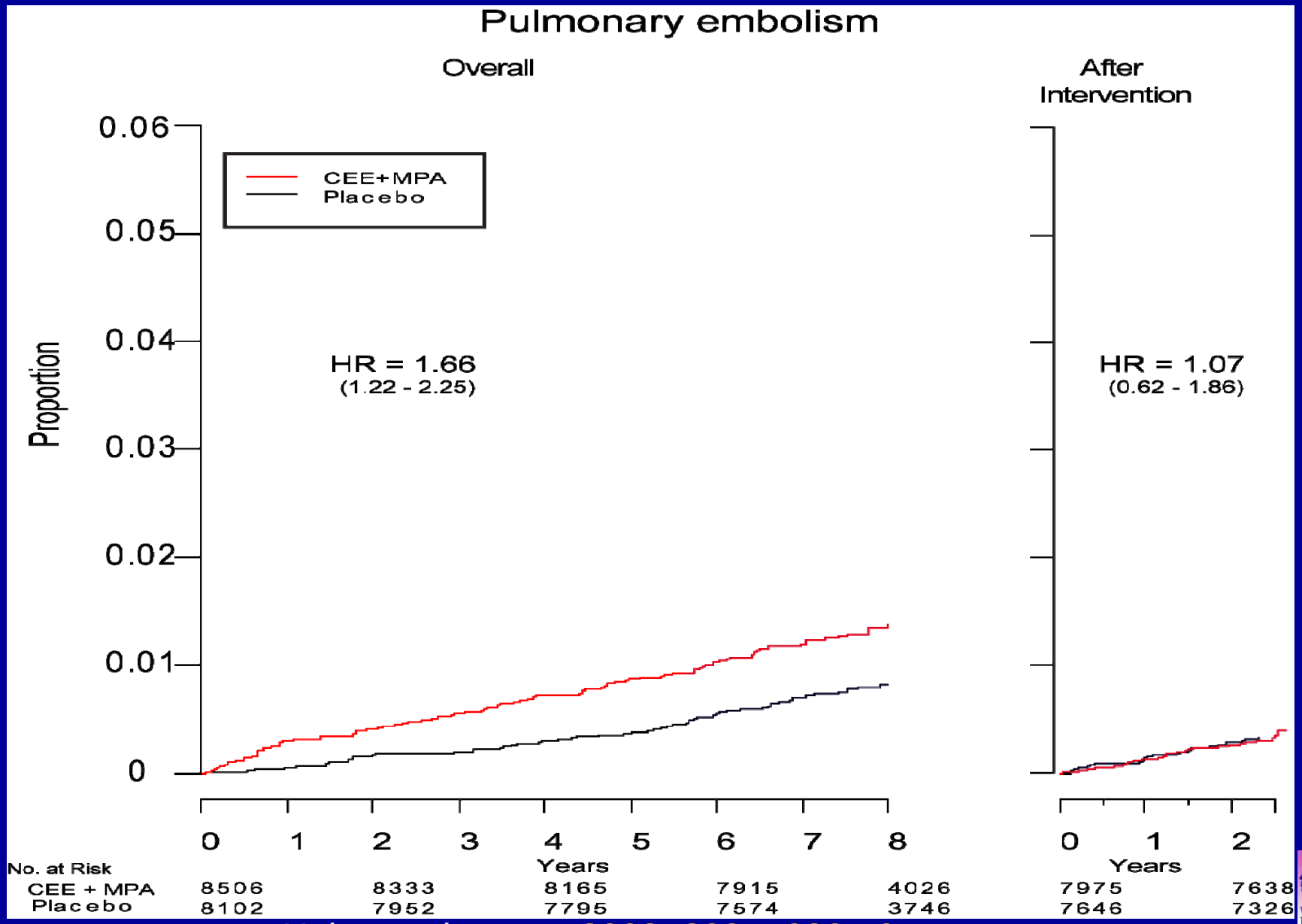
Heiss et al, **JAMA 2008; 299: 1036-1045**

WHI E+P: Post-Intervention Follow-up STROKE



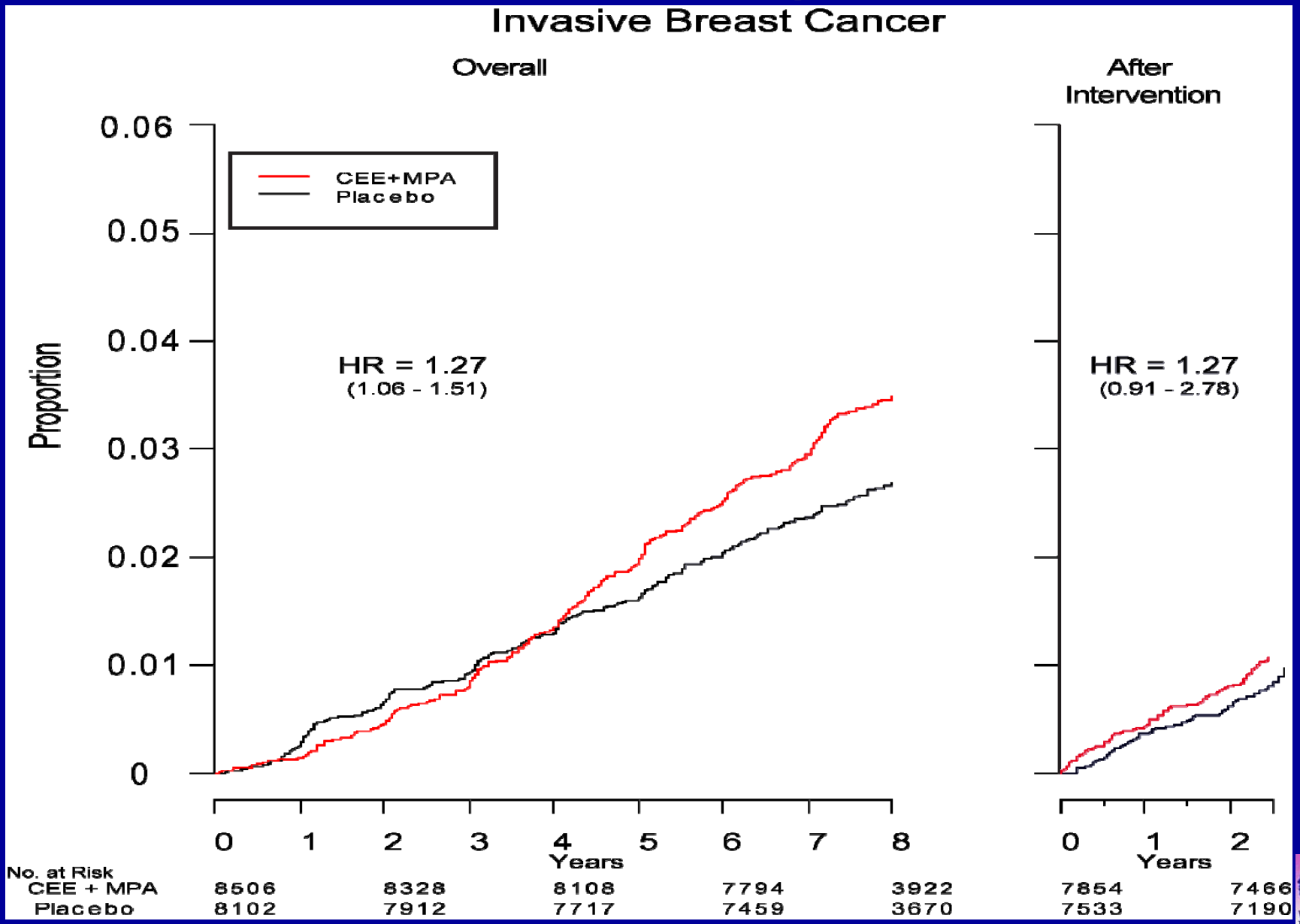
Heiss et al, **JAMA 2008; 299: 1036-1045**

WHI E+P: Post-Intervention Follow-up PE



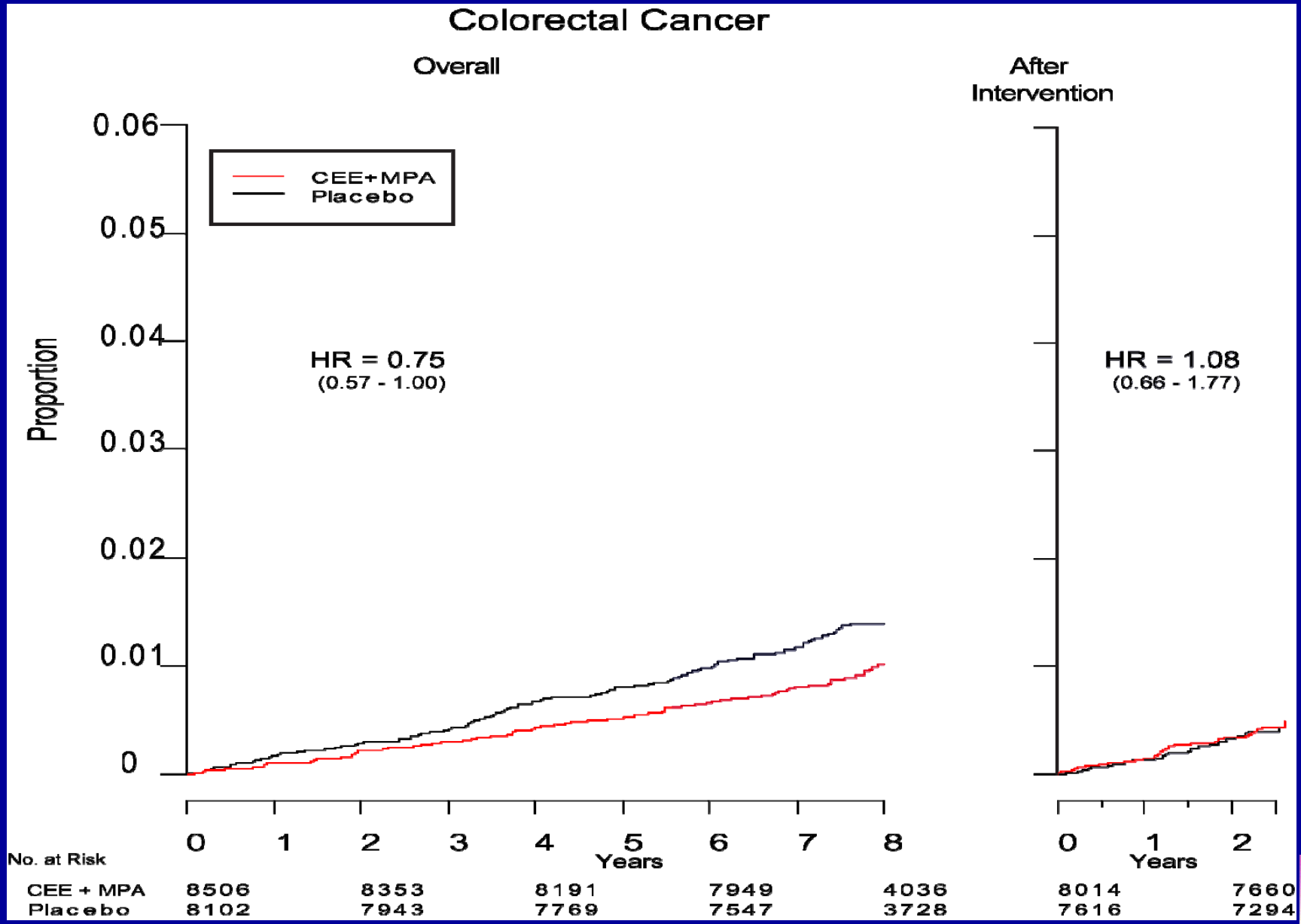
Heiss et al, **JAMA 2008; 299: 1036-1045**

WHI E+P: Post-Interv. Follow-up Breast Cancer



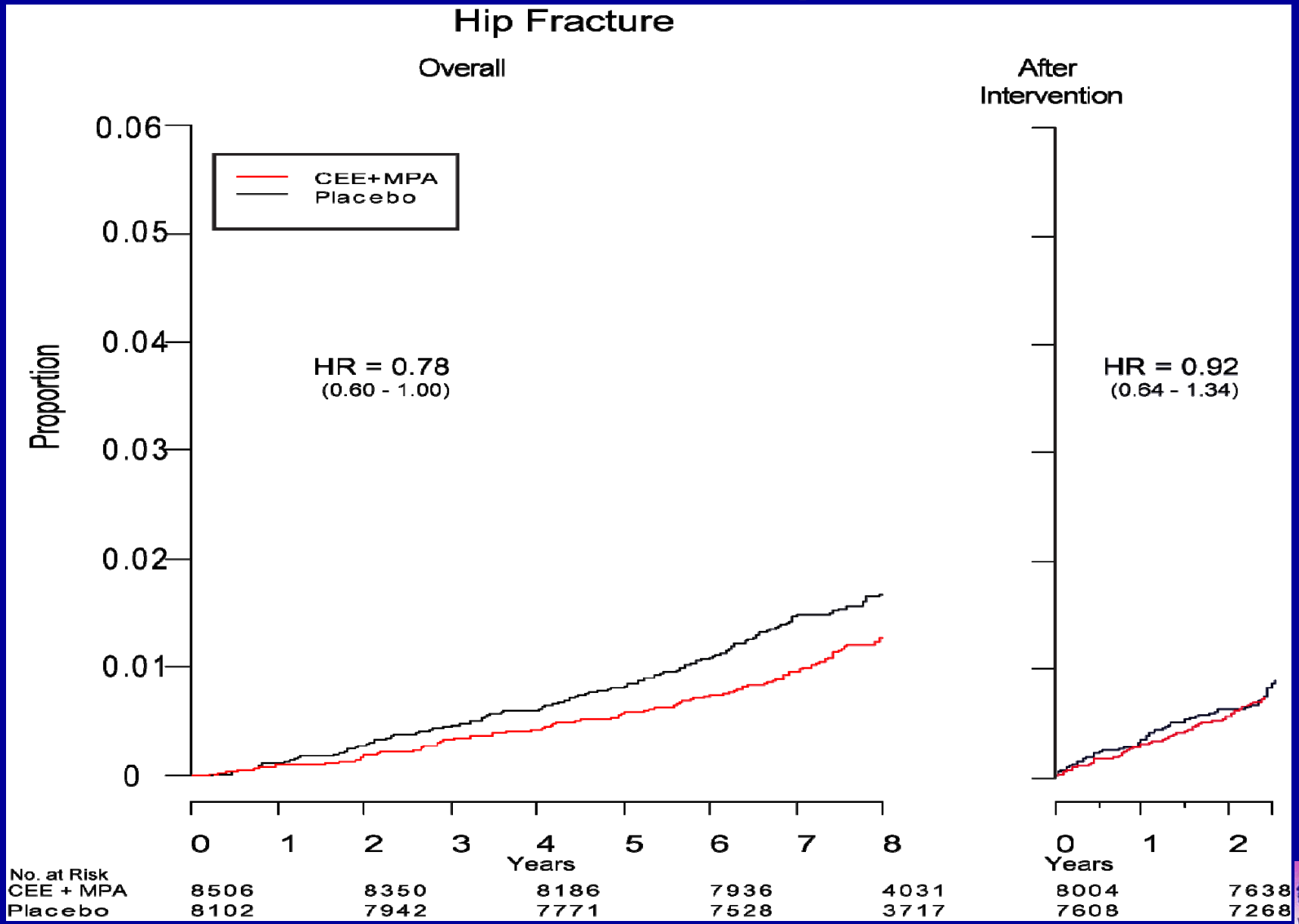
Heiss et al, **JAMA 2008; 299: 1036-1045**

WHI E+P: Post-I. Follow-up Colorectal Cancer



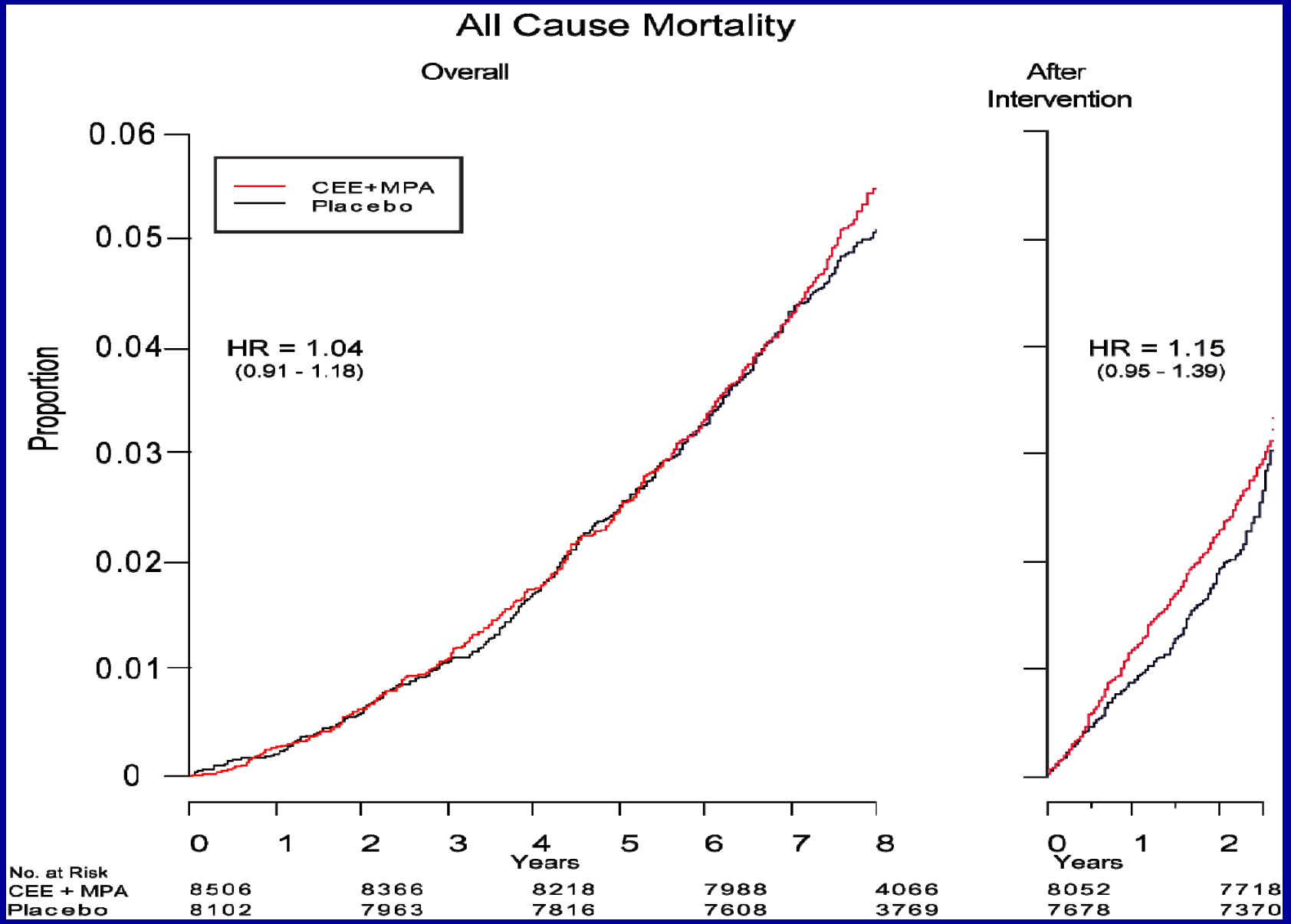
Heiss et al, **JAMA 2008; 299: 1036-1045**

WHI E+P: Post-Interv. Follow-up HIP Fracture



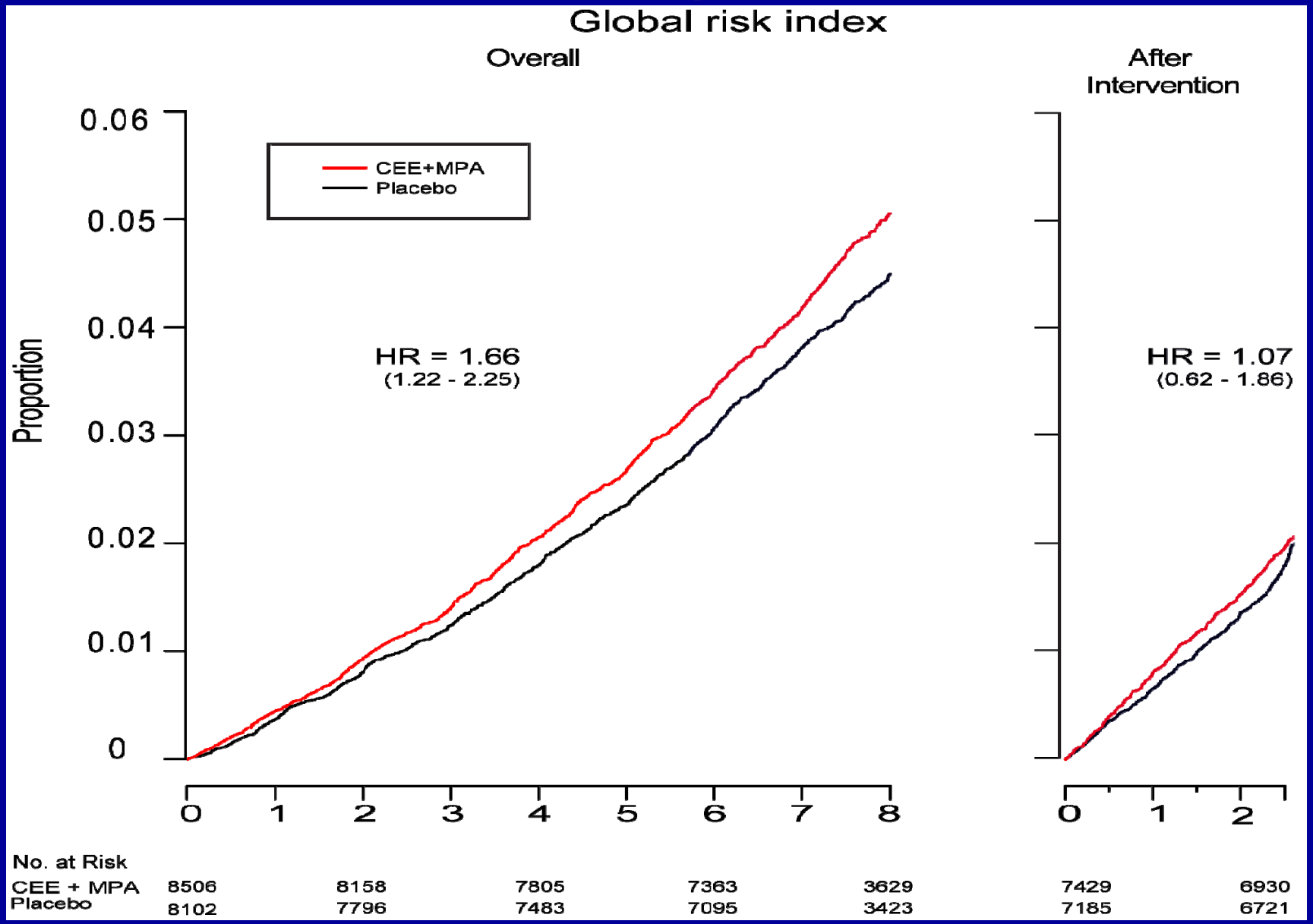
Heiss et al, **JAMA 2008; 299: 1036-1045**

WHI E+P: Post-I. Follow-up All-cause Mortality



Heiss et al, **JAMA 2008; 299: 1036-1045**

WHI E+P: Post-I. Follow-up Global Index



Heiss et al, **JAMA 2008; 299: 1036-1045**

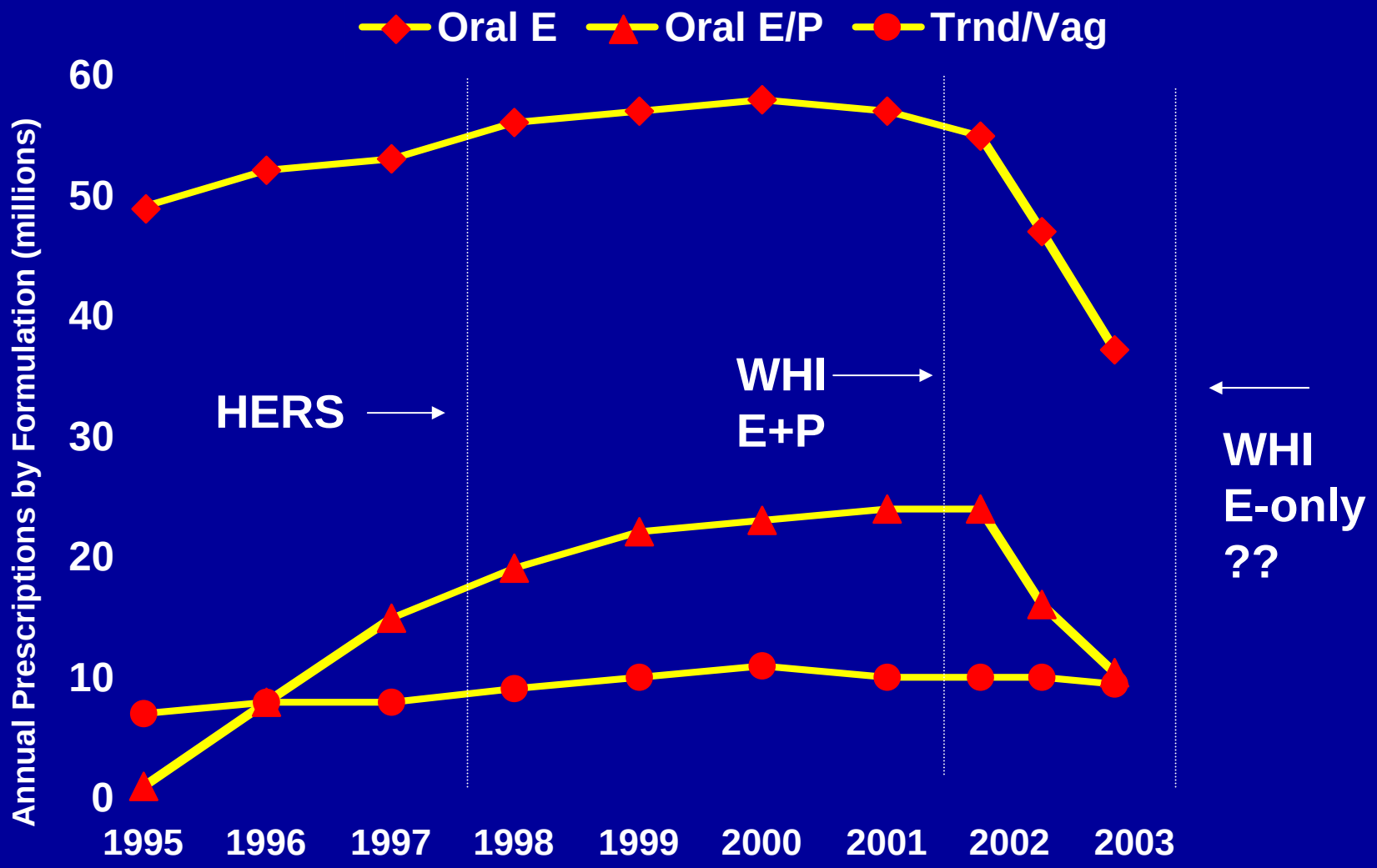
WHI E+P: Post-Intervention Follow-up

- **Cardiovascular risks disappeared**
  - **CHD, Stroke, Blood Clots – no longer increased**
- **Fracture benefits disappeared**
  - **Hip Fracture - no longer decreased**
- **Cancer**
  - **Breast Cancer - 27%** (ns) **more diagnosed post-Int.**
  - **Colorectal Cancer - no longer decreased**
  - **TOTAL CANCER - increased 1.24 (1.04-1.48)**
    - **Due to increase in variety of cancers,** including **Lung Cancer (E+P: 33** events vs **placebo:15)**
- **All-cause Mortality -15%** (ns) **higher**
  - **Most due to Cancer (E+P: 101** vs **placebo: 69)**
    - **only 27 (E+P)** and **16 (placebo) due to pre-specified CA**

Heiss et al, **JAMA 2008; 299: 1036-1045**

WOMEN'S HEALTH INITIATIVE

Annual Number of US Prescriptions for HT 1995 - Aug 2003



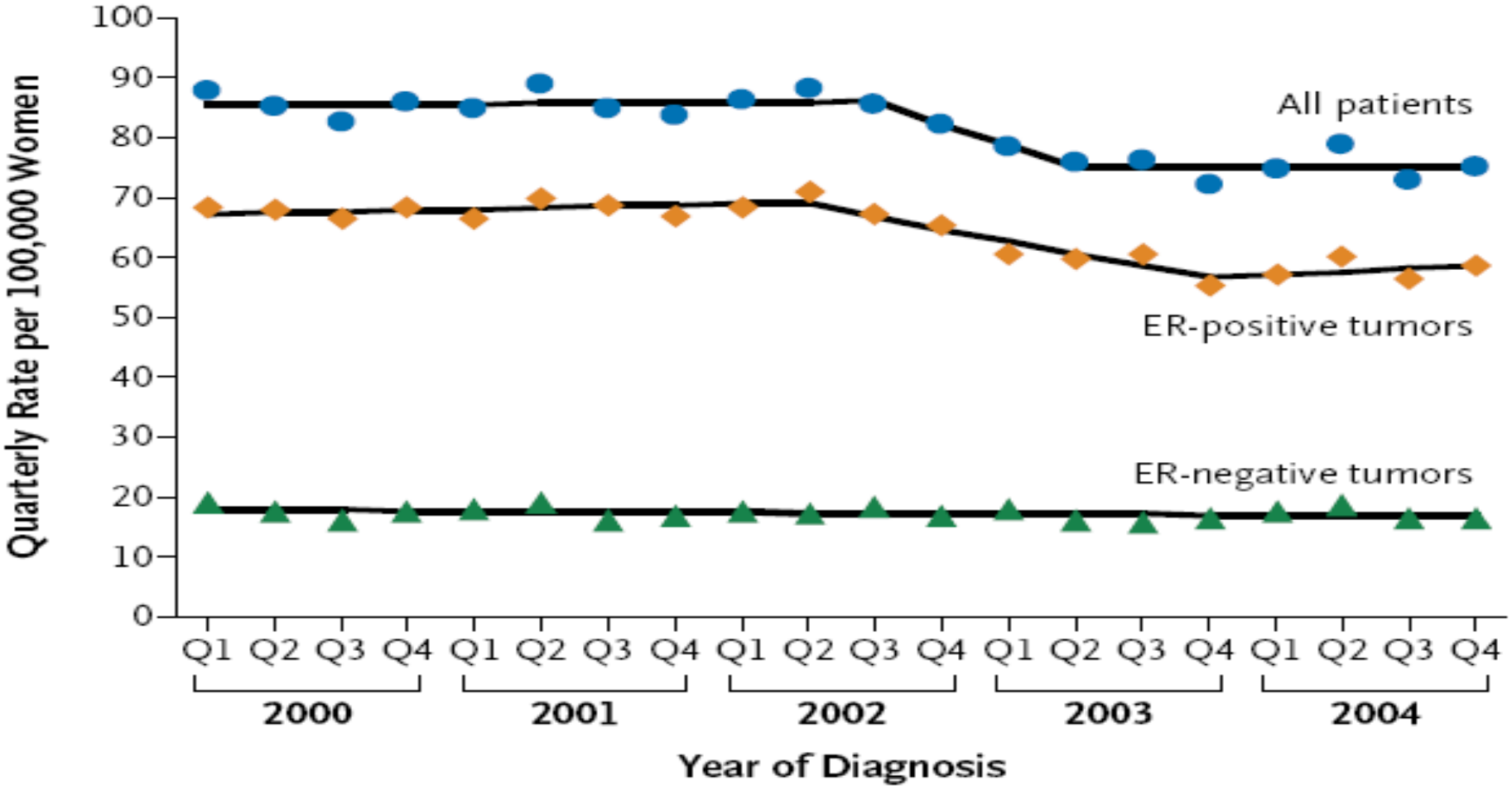
Source: IMS Health NPA Plus

Hersh AL, Stefanick ML, Stafford RS JAMA 291: 2004; 291: 47-53

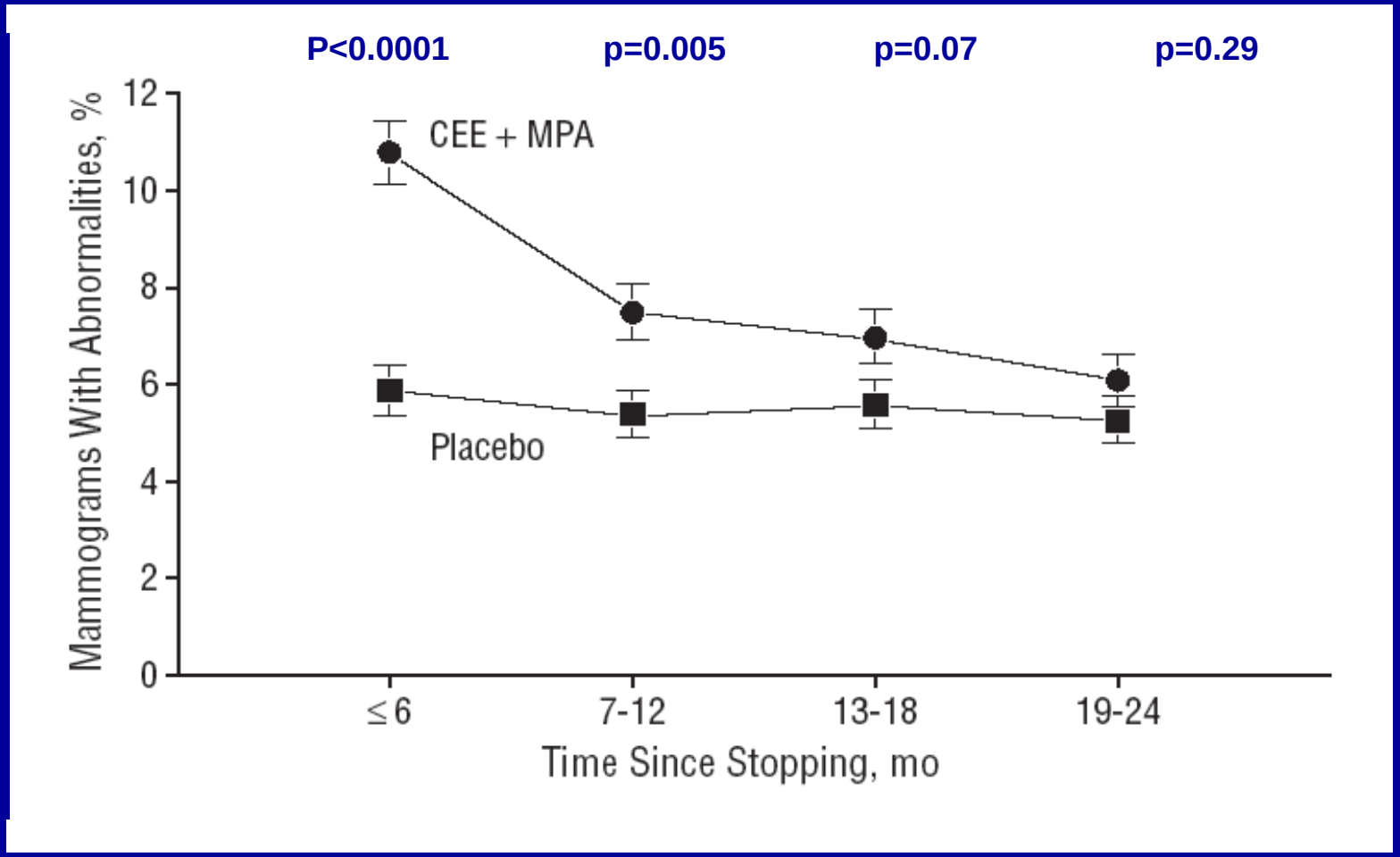
The Decrease in Breast-Cancer Incidence in 2003 in the United States

Peter M. Ravdin, Ph.D., M.D., Kathleen A. Cronin, Ph.D., Nadia Howlader, M.S., Christine D. Berg, M.D., Rowan T. Chlebowski, M.D., Ph.D., Eric J. Feuer, Ph.D., Brenda K. Edwards, Ph.D., and Donald A. Berry, Ph.D.

N ENGL J MED 356;16 WWW.NEJM.ORG APRIL 19, 2007



Mammographic Findings After the Trial Intervention Stopped: By Time Interval and Randomization Group



Chlebowski *et al*, Arch Intern Med 2008;168(4):370-377

WHI E+P: Post-Intervention Follow-up

Breast Cancer

- **Breast Cancer - 27%** (ns) **more diagnosed post-Int.**
  - "The trend of increasing risk of breast cancer during the intervention phase is seen not to extend beyond the termination of the intervention"
  - "We lacked statistical power to identify a decrease in breast cancer of the order of 9% to 10% observed in national data "
- Evidence from WHI, supporting the hypothesis generated from national data that stopping MHT results in decreased breast cancer risk, is under review & will soon be presented at a national meeting.
- **Chlebowski RT, Kuller L, Prentice R, et al. SABCS 2008, Abstract 64**

WOMEN'S HEALTH INITIATIVE

Personal Perspective: to optimize health across a woman's lifespan, focus on a "healthy" lifestyle

- Be physically active
- Maintain a healthy weight

  - Consume vegetables, fruits, & whole grains
  - Restrict saturated fat
  - Limit Salt (~1 tsp/day)
- Adequate calcium/vitamin D
- Limit alcohol intake (1*-2** drinks/d)
  - * women, ** men
- Minimize stress
- Get enough sleep
- Monitor & manage risk factors
- Do not use Menopausal Hormones for the Prevention of cardiovascular disease