

Ultima Hora!

Comentários de

Manuel Neves-e-Castro

***Presidente Honorário e Fundador
da Sociedade Portuguesa de Menopausa***

Porto, 17 Abril 2004

The published studies

- . Nurse's Health Study
- . HERS 1 and 2
- . WHI
- . ERAS
- . Oxford Breast Cancer
- . Million Women

The recommendations of the WHI writing group are mainly focused on public rather than individual health

“Those data describe increased risk of an entire population, NOT the increased risk for individual women”

Rossouw J. Release of the Results of the Estrogen Plus Progestin Trial of the Women's Health Initiative: Findings and Implication. Press Conference Remarks July 9, 2002
<http://www.nhlbi.nih.gov/whi/hrtupd/roussouw.htm>

If Absolute Risks are plotted as percentages,

instead of the additional

8 strokes

7 heart attacks

8 breast cancers ***per 10.000 woman/year***

one would have, respectively

0.08

0.07

0.08

cases per 100 woman/year

a figure that is easier to interpret



“After careful consideration of the data, NIH has concluded that with an average of nearly 7 years of follow-up completed, estrogen alone does not appear to affect (either increase or decrease) heart disease, a key question of the study. At the same time, estrogen alone appears to increase the risk of stroke and decrease the risk of hip fracture. It has not increased the risk of breast cancer during the time period of the study”

March 2,2004

The estrogen-alone study involved 40 clinical centers and 10,739 generally healthy postmenopausal women ages 50-79 who did not have a uterus. **Their average age at enrollment was nearly 64 and about 70 when the study stopped.** They enrolled in the study between 1993 and 1998.

NIH NEWS, April 13, 2004

HRT cancer fears eased for thousands

● Benefits outweigh risks for most women, says professor

By Mark Henderson
in Seattle,
Lewis Smith
and Oliver Wright

■ 1.7 million women in the UK use HRT

■ HRT prescriptions

risk of hip fracture, or five fewer cases. Dr Johnson said: "One of the groups that has abandoned it are the women who have hot flashes for

The dangers of HRT were overplayed, says expert

By Tim Utton
Science Reporter

HUNDREDS of thousands of women who stopped taking HRT after safety fears would be better off going back on the drug, it was claimed yesterday.

It is a third of women who were taking the hormone replacement therapy stopped abruptly 18 months ago after an influential study warned that it increased the risk of breast cancer, heart attack and stroke.

But one of the doctors behind the study said that was the wrong choice for many, struggling with menopausal symptoms. These women were now missing out on an effective treatment.

For women plagued with hot flashes, mood swings, night sweats and fatigue, the "hormone" risk to health is outweighed by the benefits of the drug, according to Professor Susan Johnson.

Professor Johnson, a gynaecologist at the University of Iowa, said: "There are many women for whom HRT continues to be an excellent choice for the treatment of menopause-related symptoms."

"We are talking about a huge benefit for hot flashes and other symptoms -

'It is still an excellent choice'

in excess of 80 per cent benefit from taking it - versus a really tiny risk.

But the group who have abandoned it are the women who are having hot flashes.

"And a lot of these women have done so prematurely."

"In my clinical practice, I'm pulling a lot of women back on HRT."

Her comments, made at the biggest scientific conference in the U.S., form the latest chapter in the controversy.



CASE STUDY

Scares made me halve my dosage

CAROLINE NEVILLE, 61, began to take HRT after getting pains in her knees and hips when her menopause started at 52.

The chairman of the public relations agency Neville McCarthy Associates and president of Cosmetic Executive Women UK said: "The worst menopausal symptoms were sore joints and irritability. I think I have calmed down now with HRT. I'm less liable to fly off the handle. When you have a demanding career, you've got to have energy."

"The pains in my knee joints meant I was tossing and turning at night. Having separate beds, however, is the death knell for a relationship - and I'm happy to say that my husband wouldn't hear of it."

"I tried HRT pills and patches at first, which didn't suit me."

"But after being prescribed a body cream, I immediately felt 200 per cent better. Then my husband became so alarmed by the recent health scares that I took a two-week break from it, only to find that the knee pains came back. I've compromised by reducing the amount of cream I use by half."

"I feel it's unfair of some doctors to label HRT a lifestyle drug. I think they are saying women don't need it for medical reasons."

"But I'm of the school that says there are people who wouldn't be alive if they weren't taking drugs, and I don't fool around with alternative remedies."

"I'm looking to the Government to say something on the subject of HRT."

“There are many women for whom HRT continuous to be an excellent choice for the treatment of menopause-related symptoms.”

*“In my clinical practice,
I’m putting a lot of women
back on HRT”.*

Susan Johnson *American Association for the Advancement of Science, 2004 (WHI Investigator)*



March 3, 2004

Estrogen Study Stopped Early Because of Slight Stroke Risk

By DENISE GRADY

A large federal study of estrogen therapy in postmenopausal women has been stopped a year ahead of schedule because the hormone increased the risk of stroke and offered no protection against heart disease, the government announced yesterday.

The study included only women taking estrogen alone, not those who take combined hormones. An earlier study, halted abruptly in 2002 after the researchers found an increased risk of breast cancer, involved only women taking the combined hormones estrogen and progestin.

The National Institutes of Health, which sponsored the estrogen study, part of the Women's Health Initiative, said it stopped the study because "an increased risk of stroke is not acceptable in healthy women in a research study."

03.03.2004

THE FINANCIAL TIMES

Researchers stop estrogen study over stroke fears

By Christopher Bowe
in New York

Initiative research on long-term hormone replacement therapy for post-meno-

focus of the second part, which sought to explore previous theories that hor-

Now women on HRT are warned they face higher risk of stroke

By **Jenny Hope**
Medical Correspondent

HUNDREDS of thousands of women using HRT were dealt another blow yesterday when

surgically removed can take oestrogen-only HRT. Around 60,000 hysterectomies are performed in Britain each year.

Like many women who have taken oestrogen-only HRT, 63-year-old Elizabeth Christie has been alarmed by the health risks.

Hormone Replacement Therapy: Dangerous Side Effects

[Home](#) [HRT Explained](#) [HRT Health Risks & Study Findings](#) [Free Legal Consultation](#)

Have you or a loved one have suffered due to Hormone Replacement Therapy (HRT) drugs? Our lawyers will help you get the compensation you deserve.



Study

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Related Diseases

The Women's Health Initiative study showed that combined hormone replacement therapy (estrogen plus progestin) such as Prempro and Premarin with a progestin increases the risk of the following diseases and disorders:

- Lobular breast cancer
- Ductal breast cancer
- Coronary heart disease
- Stroke
- Blood clots/deep vein thrombosis/ pulmonary embolism
- Ovarian cancer
- Dementia
- Scleroderma
- Lupus

[read more](#)

Warning: Hormone Replacement Therapy (HRT) Linked with Elevated Risk of Dangerous Diseases

Between 20 percent and 50 percent of women in the Western world who are between the ages of 45 and 70 have taken or are now taking Hormone Replacement Therapy drugs. In the past they were prescribed to every woman who experienced unpleasant symptoms of menopause. They were even expected to decrease certain health risks. Chances are if you took HRT medications, you assumed that drug companies like Wyeth had tested the safety of the medications. You are not alone – thousands of women were led to believe that these drugs were not only safe, but that they provided health benefits.

On July 9, 2002, the National Institutes of Health (NIH) revealed that it was abruptly halting the use of Wyeth's Prempro in the Women's Health Initiative (WHI) study because of unacceptable risks associated with taking the drug. Letters were sent to study participants urging them to stop taking the drugs because they led to increased risk of breast cancer, heart disease and stroke.

The Women's Health Initiative was a \$700 million, eight year publicly funded study of Hormone Replacement Therapy. It was intended to study the BENEFITS of hormone replacement and hoped to find that drugs like Prempro and Premarin helped in the prevention of heart disease, breast and colon cancer, and osteoporosis. Instead, the risks associated with these drugs outweighed any benefits found and led to the immediate halting of the study. The findings were so shocking that the study was stopped with almost three years left to go.

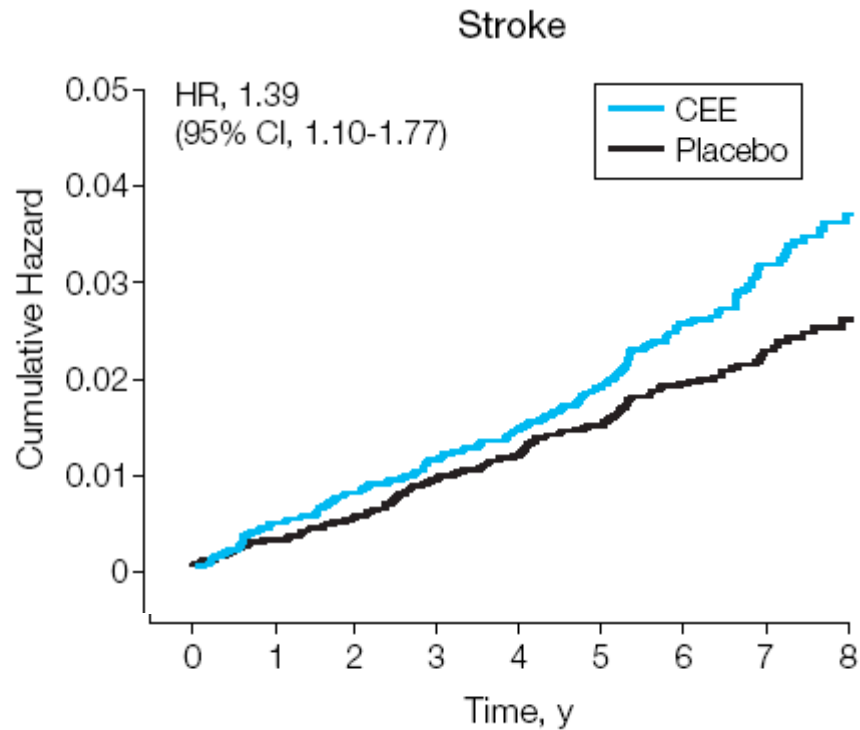
If you or a loved one took Hormone Replacement Therapy (HRT) drugs and developed any of these diseases, contact our lawyers for a free and confidential evaluation of your case. Our lawyers will help you get the compensation you deserve.

Warning: Hormone Replacement Therapy (HRT) Linked with Elevated Risk of Dangerous Diseases

If you or a loved one took Hormone Replacement Therapy (HRT) drugs and developed any of these diseases, contact our lawyers for a free and confidential evaluation of your case. Our lawyers will help you get the compensation you deserve.

Parker & Waichman 1-800-LAW-INFO (529-4636)

<http://www.hormonereplacementlawsuit.com/>



Events									
CEE	24	16	18	17	22	30	19	9	3
Placebo	15	12	22	13	15	21	11	6	3

Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712



“In that study (*WHI*), women **taking estrogen plus progestin** had **8 more strokes** per year for every 10,000 women than those taking the placebo.”

March 2, 2004

“the use of estradiol in women after ischemic stroke resulted in no change in mortality but a higher rate of recurrent nonfatal stroke”

Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712

“Similarly, in 168 women reporting prior stroke, the HR for subsequent stroke (6 vs 6; HR, 1.67; 95% CI, 0.52-5.36) did not differ from the HR in women without a history of stroke (152 vs 112; HR, 1.39; 95% CI, 1.09-1.78) ($P=.77$).”

Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712

“Another outcome that is consistent across the 3 trials is the **increased risk of stroke** among women assigned to estrogen alone or estrogen plus progestin, and this adverse effect is therefore attributable to the estrogen component of the hormone regimen. It is the only statistically significant adverse effect of estrogen alone, and **at 0.12% additional strokes per year of treatment, it is *relatively uncommon in this healthy cohort.*”**

The WHI Estrogen-Alone Trial – Do Things Look Any Better. JAMA, 2004;291:1769-1771

Effect on the risk of breast cancer

WHI Nonsignificant increased risk

RR 1.26 (CI 1.00-1.59); **26%** increased risk

AR 0.38% vs 0.30% (ie, **38** vs **30** events annually per **10.000** women)

HERS Nonsignificant increased risk

RR 1.27 (CI 0.84-1.94); 27% increased risk

AR 0.59% vs 0.47% (ie, 59 vs 47 events annually per **10.000** women)

O risco do cancro da mama aumenta com a idade

Idade (anos)	Risco
30	$\frac{1}{2}$ x
40	1 x
50	2 x
60	3 x
70	4 x

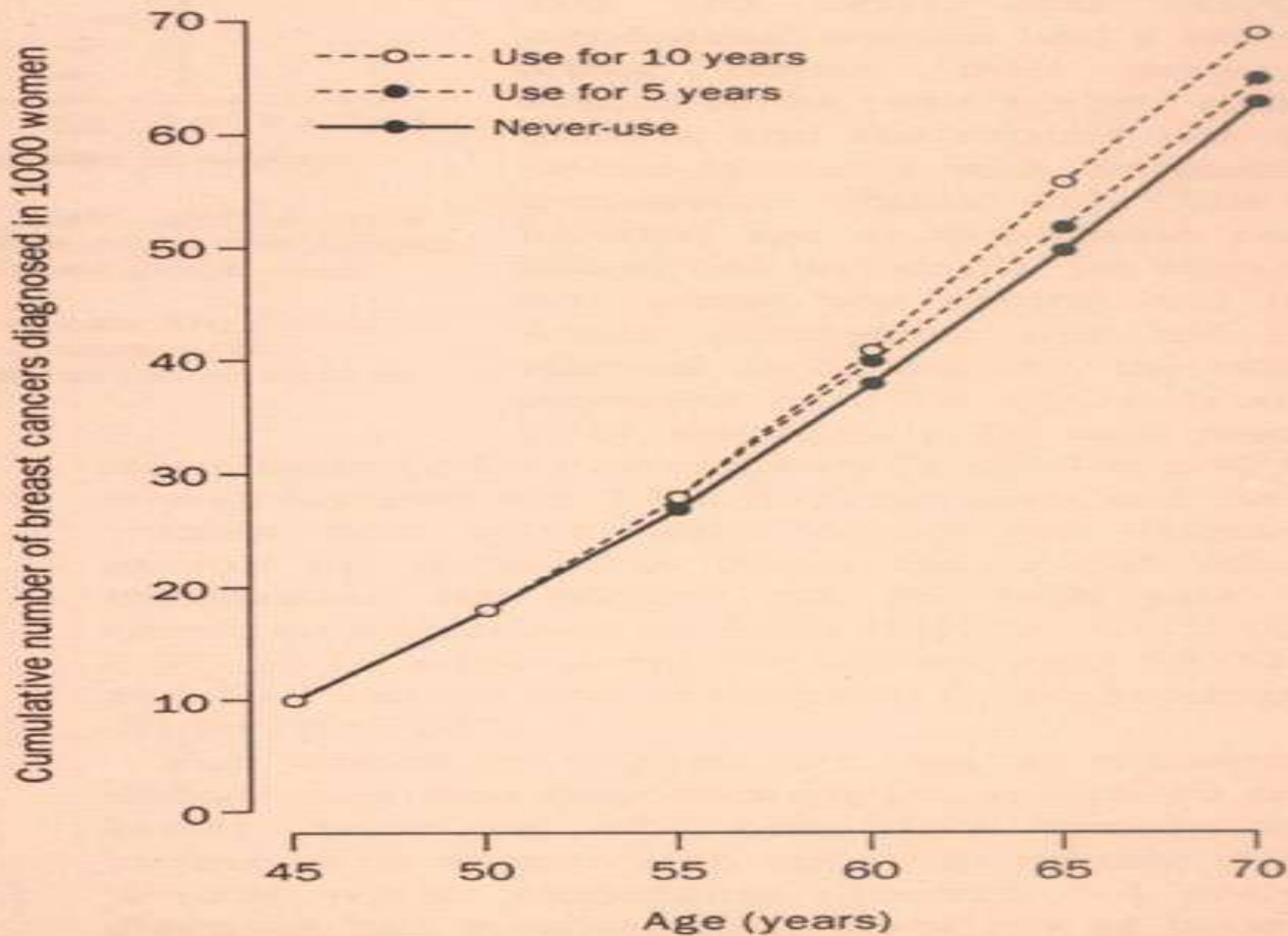


Figure 9: Estimated cumulative number of breast cancers diagnosed in 1000 never-users of HRT, 1000 users of HRT for 5 years, and 1000 users of HRT for 10 years

Estimated numbers for 1000 women in Europe or North America, with assumption that HRT use began at age 50.

HRT and breast cancer risk

	• Women with BMI < 25.0	• Women with BMI <u>></u> 25.0
• <u>Use</u> > 5 years	1.52	1.02

Conclusion: risk restricted to lean women

Beral, Lancet 1997

BREAST CANCER

<i>Risk factor</i>	<i>Relative risk</i>	<i>Increase incidence</i>
Body weight-normal weight : obesity	1 : 2.5	+ 150%
Age at menopause - 42yrs : 52 yrs	1 : 2.0	+ 100%
Age at menarche – 14 yrs: 11 yrs	1 : 1.3	+ 30%
Parity – multiparous : nulliparous	1 : 1.3	+ 30%
Age at first birth – 20 yrs : 35 yrs	1 : 1.4	+ 40%
Oral contraceptives – never user:ever user	1 : 1.1	+ 10%
<i>Hormone replacement-never:5 or more yrs</i>	1 : 1.3	+ 30%
Alcohol consumption-none:≥20 g daily	1 : 1.3	+ 30%
Serum lipids – normal : raised	1 : 1.6	+ 60%
Physical activity – activate : inactive	1 : 1.2	+ 20%

R. Santen, 2004

Million Women Study

The follow-up for breast cancer diagnosis was just over 2½ years, meaning that these breast cancers were almost certainly pre-existent at the start of the observational period.

Press Release from the *British Menopause Society*, 2003

ERRORS IN THE MWS

- * Discrepant RRs and Confidence Intervals

- *abstract

- *text

- *figures

- * Faulty Arithmetic
- * Misnamed Drugs

TOTAL: 12

ACKNOWLEDGED: 2

Nevertheless, these new data from MWS are consistent with those from WHI and other observational studies and can not be ignored. Women who are currently taking HT and especially CEPT should discuss their perceived benefits of continuing and balance these against the apparent greater risks than previously thought. There is no indication for all women to stop HT as suggested in the editorial⁹ accompanying MWS. HT remains by far the best treatment for climacteric symptoms and for many

David W Sturdee, Alastair H MacLennan. Is combined Estrogen/Progestogen Hormone Therapy worth the risk? (editorial) Climacteric, 2003;6(3):177-9

Million Women Study Breast Cancer

The authors (*MWS*) also suggest that HRT **may increase**, rather than decrease, **the risk of death from breast cancer**, a finding that is at variance with some previous studies.

Press Release from the *British Menopause Society*, 2003

Results for Breast Cancer Mortality With ET/HT Use Show Consistency

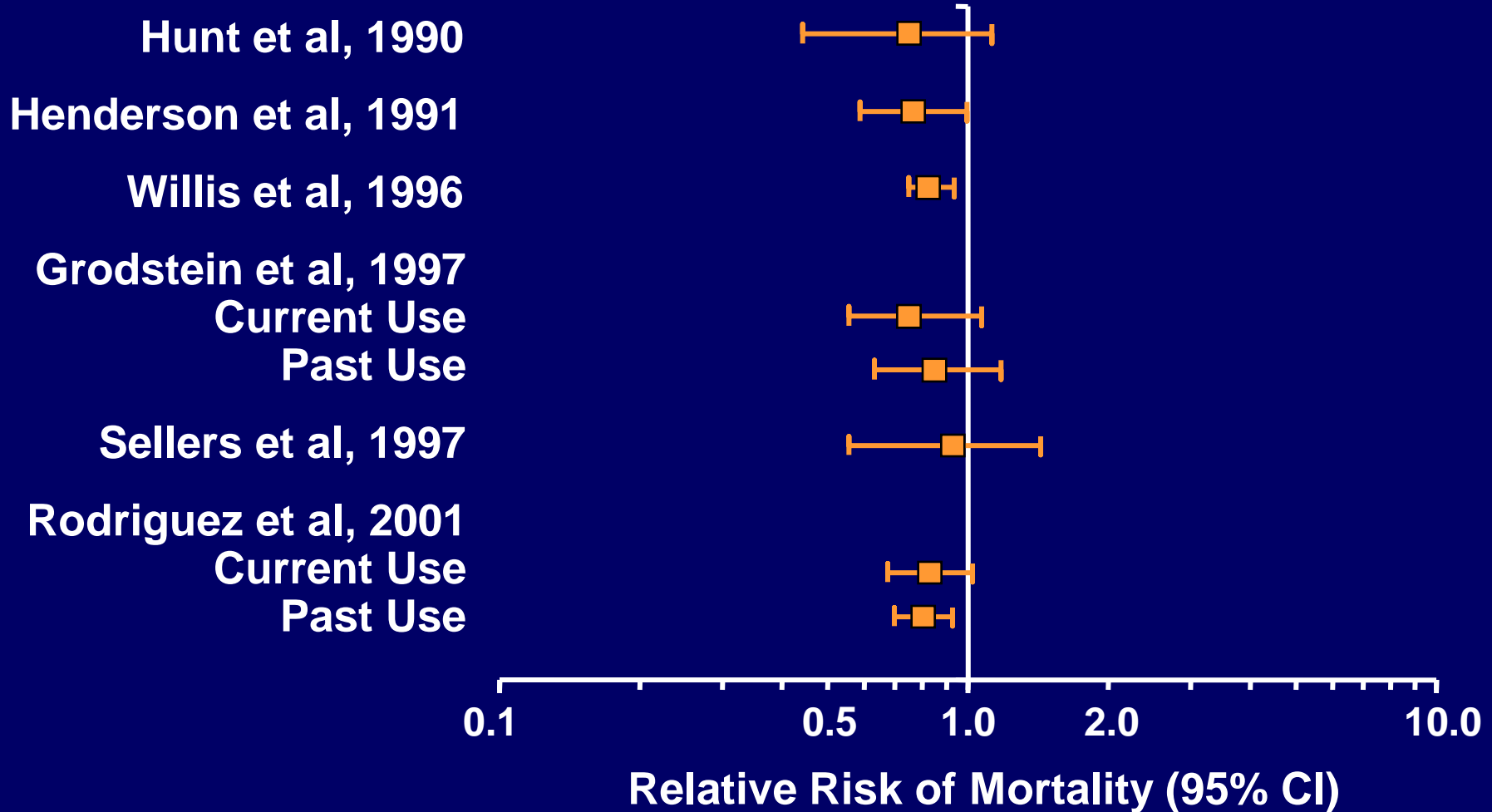
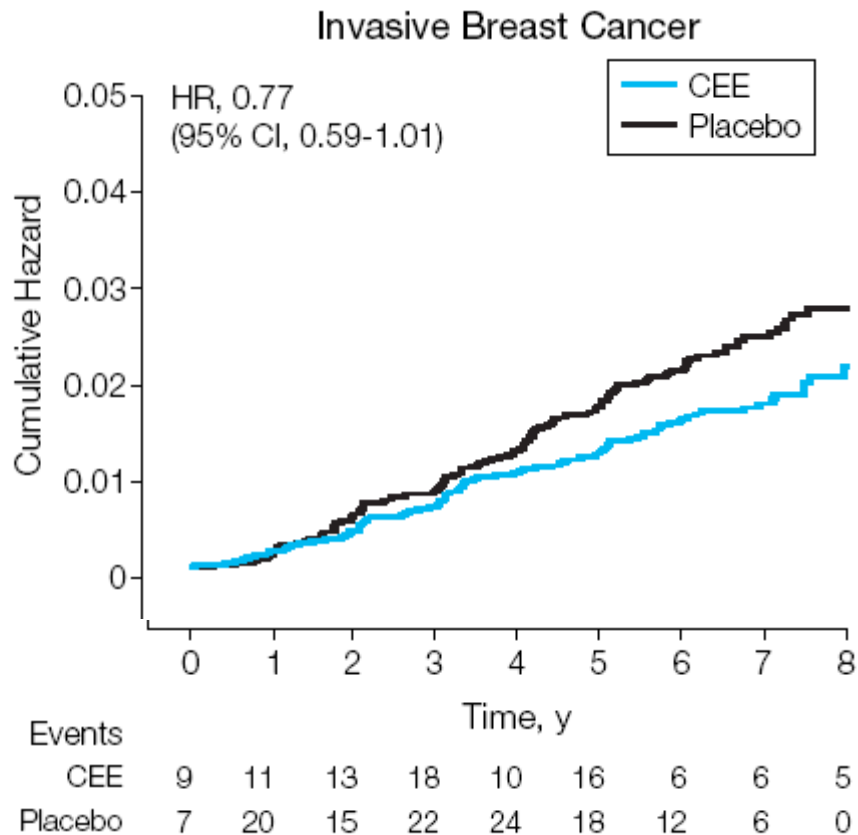


Table 4. Causes of Death

	No. (Annualized %)	
	CEE (n = 5310)	Placebo (n = 5429)
Total deaths	291 (0.81)	289 (0.78)
Adjudicated deaths	278 (0.77)	272 (0.73)
Cardiovascular	93 (0.26)	95 (0.26)
Breast cancer	4 (0.01)	8 (0.02)
Other cancer	110 (0.30)	118 (0.32)
Other known cause	51 (0.14)	38 (0.10)
Unknown cause	20 (0.06)	13 (0.04)

Abbreviation: CEE, conjugated equine estrogen.

Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712



Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712

Colorectal Cancer

50-59	8 (0.07)	14 (0.12)	0.59 (0.25-1.41)
60-69	26 (0.16)	31 (0.19)	0.88 (0.52-1.48)
70-79	27 (0.32)	13 (0.15)	2.09 (1.08-4.04)

.048

Hip Fracture

50-59	5 (0.04)	1 (0.01)	5.04 (0.59-43.17)
60-69	6 (0.04)	19 (0.11)	0.33 (0.13-0.83)
70-79	27 (0.32)	44 (0.52)	0.62 (0.38-1.00)

.39

Total Death

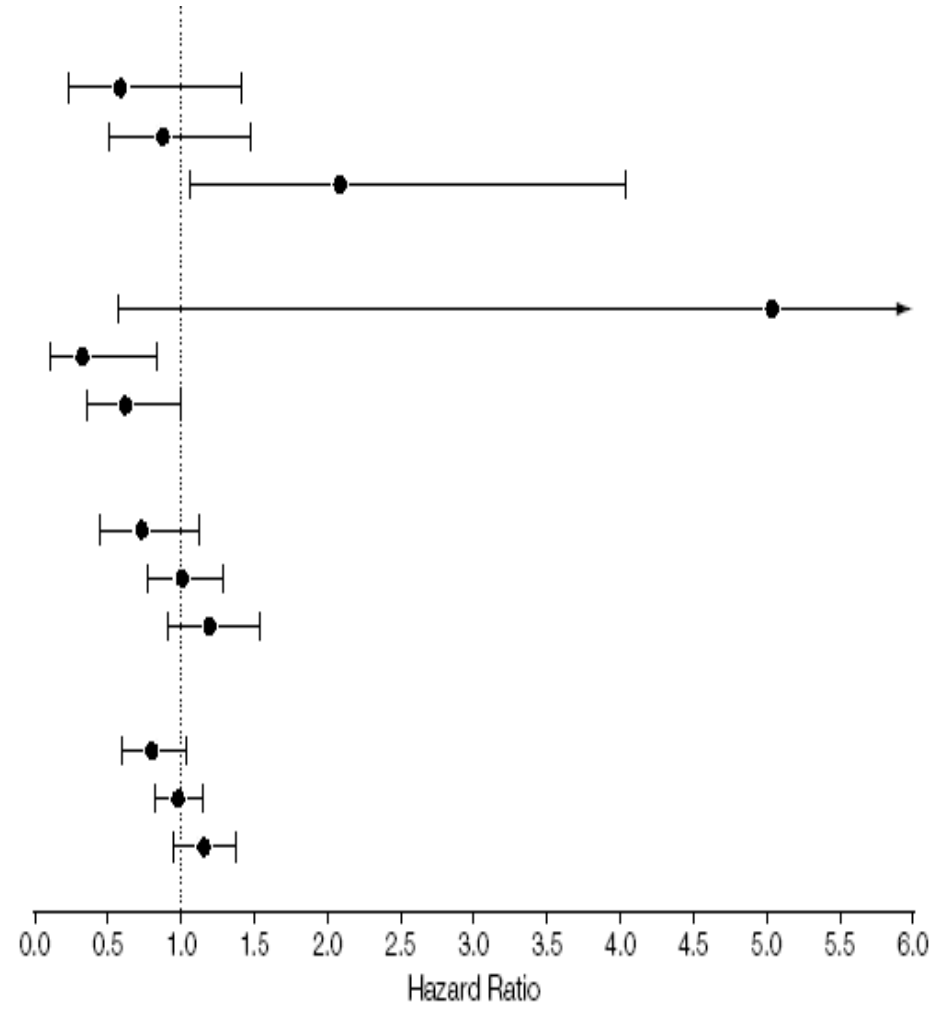
50-59	34 (0.29)	47 (0.39)	0.73 (0.47-1.13)
60-69	127 (0.79)	131 (0.79)	1.01 (0.79-1.29)
70-79	130 (1.54)	111 (1.30)	1.20 (0.93-1.54)

.19

Global Index

50-59	104 (0.89)	132 (1.11)	0.80 (0.62-1.03)
60-69	312 (1.95)	327 (1.97)	0.98 (0.84-1.15)
70-79	276 (3.28)	246 (2.88)	1.16 (0.97-1.37)

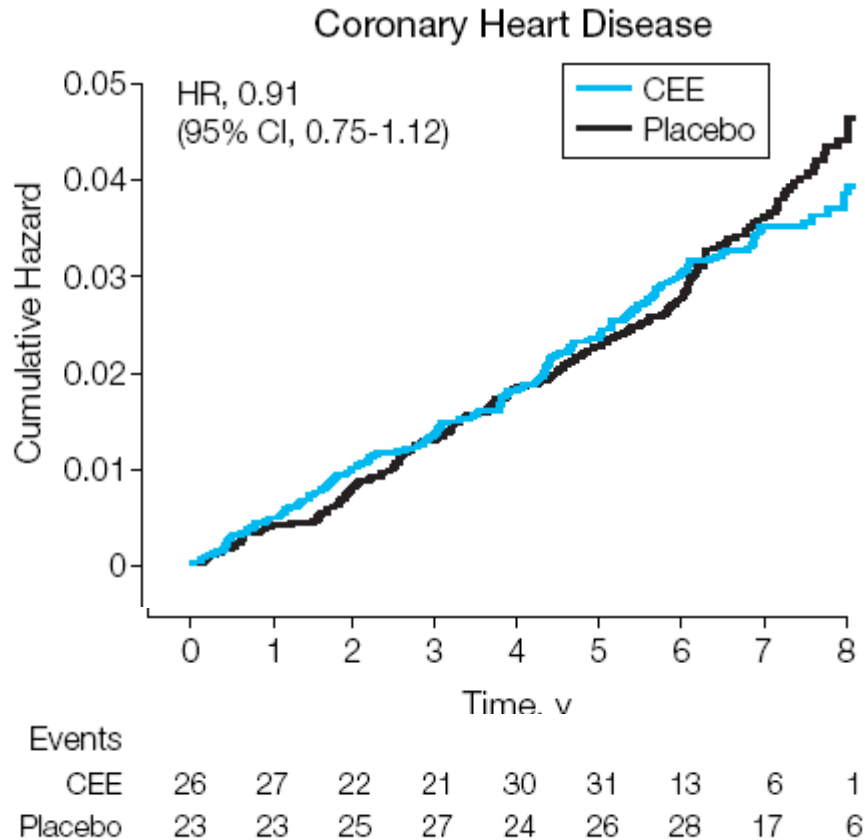
.08



Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712

“The results make clear that hormone therapy does not protect women against coronary heart disease and increases their risk for stroke,” *said Dr. Jacques Rossouw, WHI Project Officer at NHLBI.* “This may be especially true for older women, such as those aged 60 and older in this study.”

NIH NEWS, April 13, 2004



Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712

“Among the 441 women enrolled with prior MI or revascularization procedures, the effect of CEE relative to placebo (33 vs 31; HR, 1.04; 95% CI, 0.63-1.71) did not differ significantly from the CEE effect in women without documented CHD (143 vs 162; HR, 0.91; 95% CI, 0.73-1.14) ($P = .55$).”

Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712

“In all 3 major trials, the **mean age of participants was in the mid-60s**, raising the concern that *these results may not apply to treatment begun early in menopause*. In this regard, the WHI estrogen-alone trial found that the subgroup of women in the youngest decade (aged 50-59 years) appeared to respond to estrogen more favorably than older women for many of the outcomes”

The WHI Estrogen-Alone Trial – Do Things Look Any Better. JAMA, 2004;291:1769-1771

“In preliminary subgroup analyses, the estimated HRs for CEE for several monitored outcomes, including the global index, were lower for women aged 50 to 59 years”

Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712

**“CEE may be somewhat more favorable
in younger than in older women”**

*Effects of conjugated Equine Estrogen in Postmenopausal Women
with Hysterectomy. JAMA, 2004;291:1701-1712*

Statement from the Council on Hormone Education on the Results of the Estrogen-Only Study of the WHI

The current results are favorable for younger postmenopausal women in terms of no increase in CHD, a decrease in breast cancer incidence, and a reduction in hip fractures. Because **this study was carried out in older women**, the Council encourages more refined trials in a younger aged population.

April 15, 2004. sriley@dwrite.com

Evaluation of Cardiovascular Event rates with Hormone Therapy in Healthy, Early Postmenopausal Women

“Our data of no observed events in the 2 clinical trials suggests that there is no increased risk of CHD in this younger, healthy population of symptomatic women”.

Evaluation of Cardiovascular Event rates with Hormone Therapy in Healthy, Early Postmenopausal Women

“These data seem to suggest that the results of early CHD risk observed in WHI may not be applicable to healthy, younger postmenopausal women who seek treatment for menopausal symptoms”.

The conclusions of these studies suggest that the “*safe*” woman (NNH between 600-1000 women) to initiate HT is

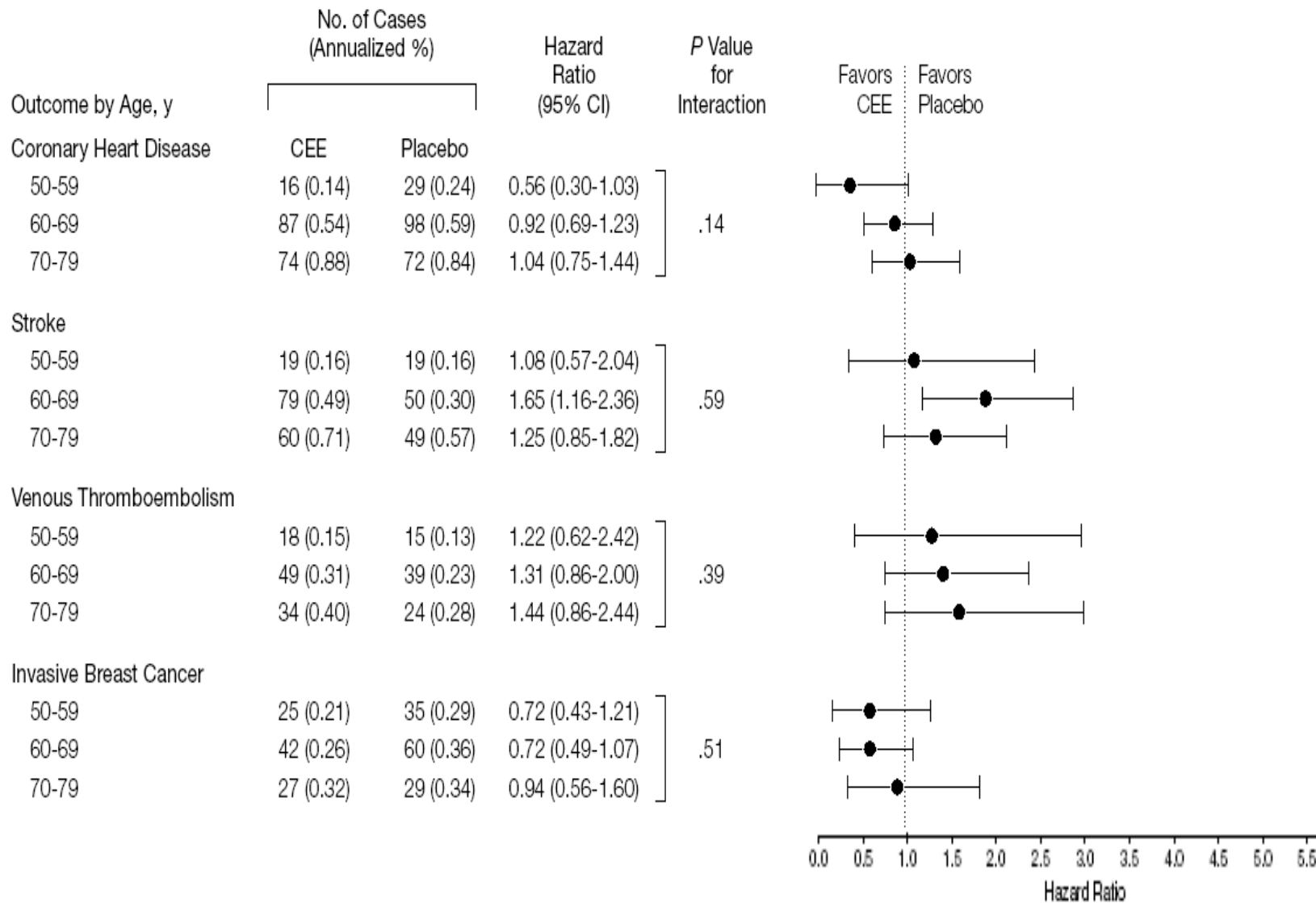
- between 50-59 years of age
- with vasomotor symptoms
- less than 10 years after the menopause
- being treated with statins
- with a good lipid profile and
- with a Body Mass Index >25

Neves-e-Castro M. Menopause in crisis post-Women’s Health Initiative? A view based on personal clinical experience.

Human Reproduction 2003;18:1-7

“Women considering taking CEE should be counseled about an *increased risk of stroke* but can be reassured about no excess risk of heart disease or breast cancer for at least 6.8 years of use.”

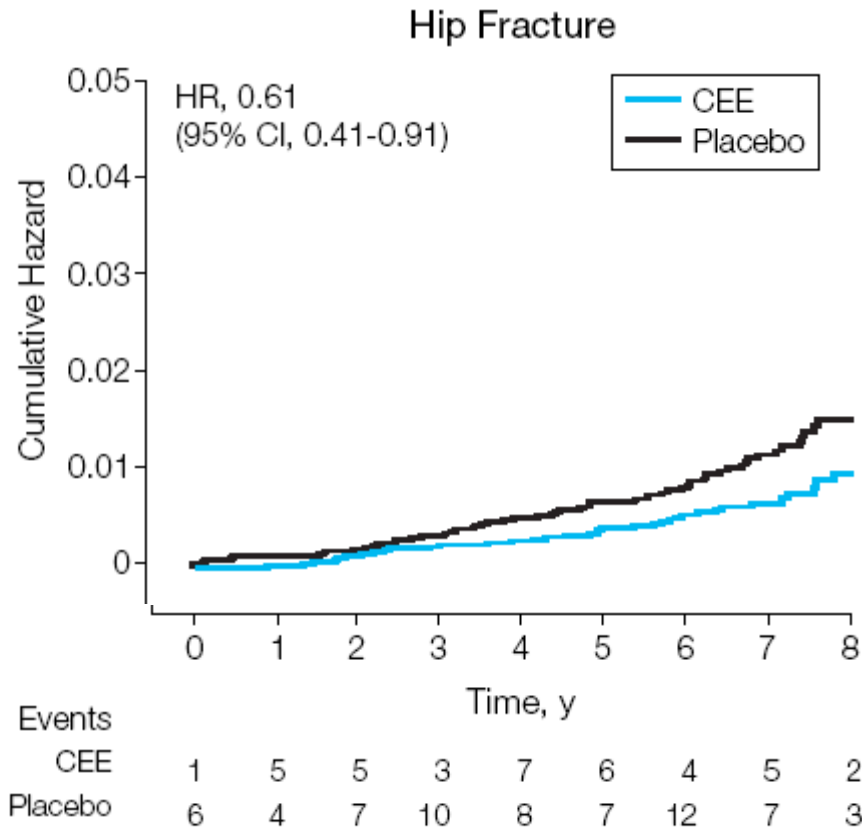
Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712



Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712

The WHI estrogen-alone trial provides strong evidence that CEE reduces the risk of hip, clinical vertebral, and other fractures.

Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712



Effects of conjugated Equine Estrogen in Postmenopausal Women with Hysterectomy. JAMA, 2004;291:1701-1712

E depois de todas estas querelas ...

e **lobbies**... (*SERM's, bisfosfonatos, fitoestrogénios*)

a TIBOLONA continua incólume ...

porque...

- **Protege** o ôsso
- **Protege** a mama
- **Melhora** o humor
- **Melhora** a libido
- **Não lesa** o sistema cardiovascular
- **Não estimula** o útero
- **É SEGURA**
- **É EFICAZ**

Quando será que o **INFARMED**
tem a **inteligência** e a **independência** suficiente
para **perceber**
que tem o dever
de aprovar *uma participação*
para o **LIVIAL**
a que as Mulheres têm direito?

Mais uma pergunta incômoda...do Manuel Neves-e-Castro