

# Tratamentos Hormonais

Porque sim?

Porque não?

*por*

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da

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# To Know ...

## *What is it?*

It is the selective and critical acquisition of information and its concerted integration in our mind.

Are we being well **informed**?

or

“well” **misinformed**? ...

# Information is based on Epidemiological studies

- How were they performed?
- What similarities do they have with our clinical practice?
- How to interpret them?

# Epidemiological studies

- 1. Descriptive studies**
- 2. Analytical studies**
- 3. Experimental studies**

# 1. Descriptive Studies

- **Who** has the disease?
- **What** is the disease?
- **Why** did the condition arise?
- **When** does the disease occur?
- **Where** does the diseases occur?
- **What** is the clinical importance of report?

# 2. Analytical Studies

- Cross-sectional
- Observational :

***Case control*** (starts from a disease and looks back in time at exposure)

***Cohort studies*** (from exposure to outcome; natural history of disease)  
**(NHS)**

then ...

**How to screen**

what **is true** and

what **is not** ?...

MNC/04



# The “language” of the results

- . Absolute risks (AR)
- . Relative risks (RR)
- . Number needed to treat (NNT)
- . Number needed to harm (NNH)
- . Number needed to screen (NNS)
- . Events per woman / years (W/Y)
- . Events per total number of women

# Example of Absolute Risk

- *If you buy one lottery ticket you will have a one in 1 million chance of winning*
- *If you buy five lottery tickets your chances are five fold higher or 5 in one million*
- **Your chances of winning are increased by five fold (relative risk)**

# Relative Risk

**The risk of an event occurring under certain circumstances compared to the risk under other circumstances**

# Attributable or Excess Risk

The difference between underlying risk and risk when receiving HT is called the **attributable or excess risk**

**Do not confuse...**

***Relative Risk***

with

***Absolute Risk!***

# Conclusion

- **Relative risk** is a confusing word and is only important if the absolute chances of an event are high
- **Attributable or excess risk** is the thing that one should be most concerned about

**What is**

**a woman / year ?!**

**100 woman/years = 100 women treated during 12 months**

is it the same as

**100 woman/years = 400 women treated during 3 months**

?



# 3. Experimental Studies

- **Controlled randomized trials**  
**(WHI)**
- **Crossover trials**

# Confidence interval (C.I.)

A 95% C.I. signifies that there is a 95% chance that the population “true value” lies between the two limits.

If C.I. crosses the “line of no difference” the point at which a benefit becomes a harm (i.e.1) then one can conclude that the results are not statistically significant

Does  
“**Statistically Significant**”  
always equate to  
“**Clinically Relevant**”?

# *p* Value

Is the probability of obtaining the observed relative risk by chance

(*p* must be  $< 0.05$ )

# Type of association

- Spurious
- Indirect
- Causal

Strength of association

Consistency

Dose response relationship

Specificity

Biological plausibility

# Validity

**Internal:** the study measured what is set out to measure

**External:** the results can be extrapolated to one's patients

***Observational research (NHS)*** may have

poorer internal validity

better external validity

**Randomized controlled trial (WHI)**

better internal validity

poorer external validity

# 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)

# WHI

(*JAMA* 2002;288:321-331)

- **Results:**

“the difference reaches “almost nominal statistical significance” (*i.e. not statistically different!*)

- **Discussion:**

“the substantial risks for CVD and breast cancer” (?!...)



*Thus...*

“The breast cancer findings are reported as **statistically insignificant** but are regarded as **clinically relevant!**”

Utian W. Menopause Management 2003;12:9-10

Do not confuse...

*Morbidity*

with

*Mortality*

# Breast cancer

## WHI

RR **1.26**

ARC 0.30% / 10.000 / yr

C.I. (1.00 – 1.59)

ART 0.38% / 10.000 / yr

Attributable risk = 8/10.000 / yr

= 1/1.250 / yr

**NNH**

= **1.250 / yr**

# Breast cancer

## HERS

RR= 1.27

ARC = 0,59% / 10.000 / yr

C.I.(0,84-1.94)

ART = 0,47% / 10.000 / yr

Attributable risk = 12 / 10.000 / yr

= 1 / 833 / yr

NNH

= 833 / yr

***“The nurse’s study and ones like it could be right and the Women’s Health Initiative could be wrong, or vice-versa”***

Rossouw J, 2003

***“May be each study is wrong.  
May be estrogen, in pills, is not  
the chemical to focus on”***

Rossouw J, 2003

***“If each is right it may be because the women in the two types of studies are different in a way that researchers have not yet figured out”.***

Rossouw J, 2003

***“It is quite possible that both are correct. The different results may hinge on the differences between the women who joined the studies”***

**Grodstein F, 2003**



# Occult Breast Cancer

***Clinically occult*** in situ BC's are **frequent** in young and middle-aged women.

Nielsen M *et al*-Br J Cancer 1987;56:814-9

# Occult Breast Cancer

Breast malignancy was  
found in 22 women  
(20%)

Nielsen M *et al*-Br J Cancer 1987;56:814-9

# Occult Breast Cancer

*Malignancy was significantly more frequent among women*

- . aged more than 40 years
- . with late age at first full-term pregnancy
- . with alcohol abuse
- . with steatosis or cirrhosis of the liver

# HRT and Breast Cancer

## Pregnancy Following Breast Cancer

Gelber 2001

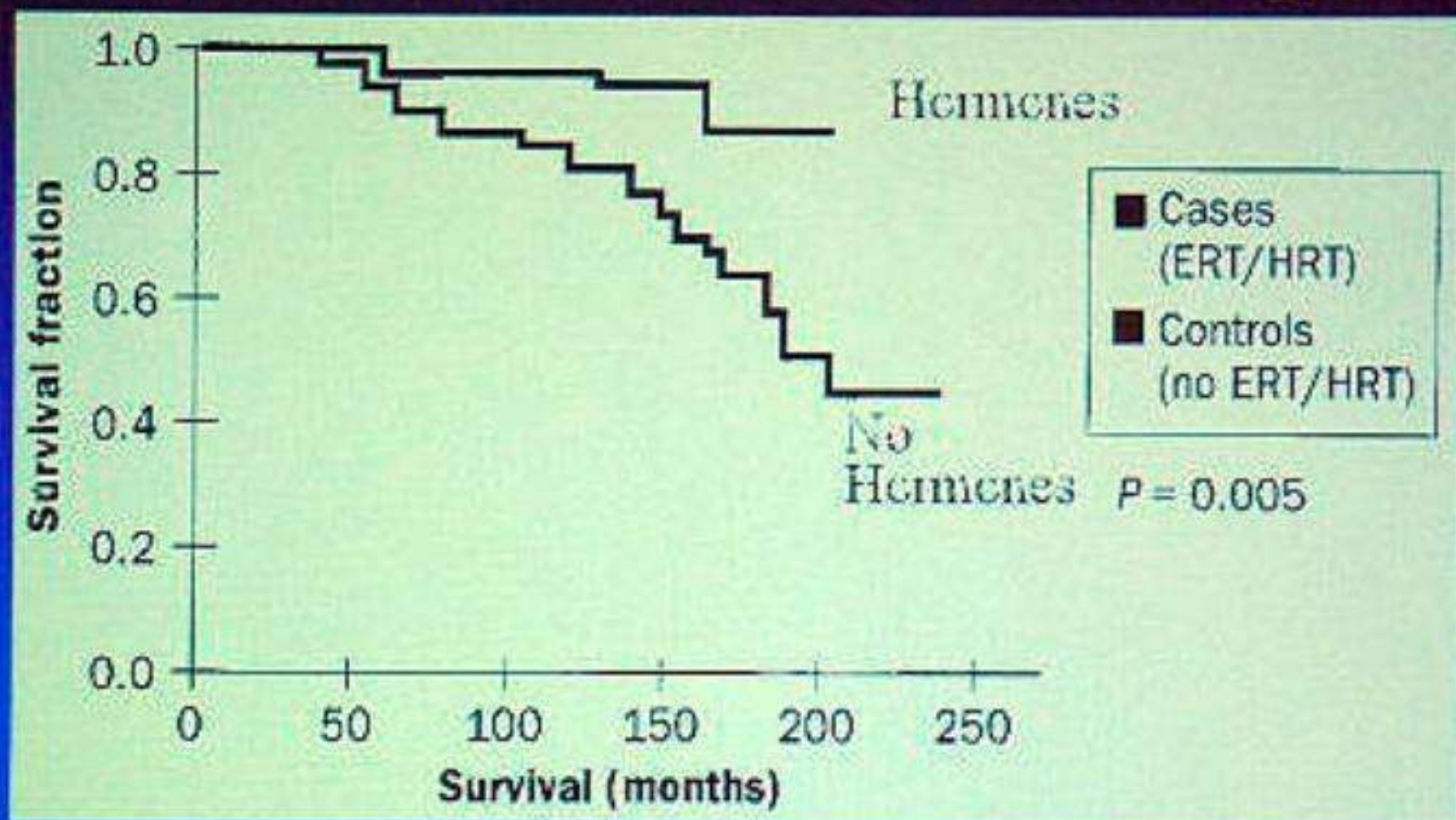
	<b>Cases</b>	<b>Controls</b>
	<b>86</b>	<b>172</b>
<b>5yr survival</b>	<b>97%</b>	<b>86%</b>
<b>10yr survival</b>	<b>93%</b>	<b>75%</b>

# HRT in Breast Survivors: results: Matched Analysis

174 breast cancer cases taking estrogen  
matched 4:1 controls with cancer not taking  
Estrogen.

	Cases (ERT/HRT)	Controls (no ERT/HRT)
recurrence	17/1000	30/1000
Br cancer deaths	5/1000	16/1000
Total deaths	16/1000	30/1000

# HRT in Breast Cancer Survivors: Results: Kaplan Meier Survival Analysis



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

This is precisely the profile of the great majority of women who come for consultation after their menopause.

Therefore *it seems that what most gynecologists are doing to their predominant population of patients is not unsafe and contributes not only to a good quality of life but to prevention, as well.*

*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*



“Each time we learn something new, the astonishment comes from the recognition that we were wrong before.

*In truth, whenever we discover a new fact, it involves the elimination of old ones.*

**WE ARE ALWAYS, as it turns out, fundamentally IN ERROR.”**

*Lewis Thomas*

*English Biologist (1913-1993)*

# The take-home message is:

(1)

Prescribe postmenopausal  
hormonal treatments

when clinically indicated,

*if not contraindicated!*

# The take-home message is:

(2)

- The prescription of long-term hormonal treatments must depend always on a benefit/risk analysis *in comparison with other non-hormonal medications and strategies.*

# The take-home message is:

## (3)

- No answers from ongoing clinical trials are indispensable to practice today a good Medicine !

MNC/02

Preventing a woman from the  
benefits of a  
**sound postmenopausal  
hormone therapy**

because of the fear of rare  
side effects

*does not seem to be  
satisfactory Medicine...*

*M.Neves-e-Castro, 2000*

# Epidemiological Studies

***PLEASE!***

Do not read only the titles...

Do not read only the abstracts...

Do read the full paper !

**Be critical!**

Make up your own mind!