LA MENOPAUSIA FUE ATACADA POR EL TERRORISMO HORMONAL !

ESTRATEGIAS PARA SU DEFENSA

POR

Manuel Neves-e-Castro

Lisboa-Portugal


Quiero hacer TH !
El Terrorista Hormonal
Pero todos los medicos dicen que NO!

Ojo al *Charqui* !

Que es el Terrorismo?

Es una acción, imprevisible y violenta, que causa daños graves tanto en las poblaciones como en los que tienen la responsabilidad de assegurar su bien-estar

Los instrumentos del Terrorismo

son algunos agentes que se intitulan detentores de la *única* verdad y que, por la fuerza de sus convicciones y armas, quieren violentamente imponerlas a las comunidades

Have they ever treated a woman? …

It is regretable that some epidemiologists, with no clinical experience, feel entitled to set the rules for clinical practice as if they were *hormone legislators !...*

They are hormone terrorists!...

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El ataque!

La comunidad medica, responsable por la salud de las mujeres, fué atacada por unos tantos terroristas-epidemiólogos que, sin experiencia clínica, han querido imponer su nueva verdad sobre el uso de las hormonas en la menopausia

The Encyclicals…

"What is especially worrying about the statements and presribing encyclicals is the apparent blinkered belief in the infallibility of the WHI and the MWS"

Sturdee D and MacLennan A –(Editorial) Should epidemiology,the media and quangos determine clinical practice? ***Climacteric 2004;7:1-2***

Sin reglas del juego…

Los observadores **de muchos paises desde luego se han dado cuenta que estes terroristas no sabian cumplir las reglas del juego que son adoptadas por los que honestamente quieren transmitir las autenticas verdades…**

Los manifestos pamfletários…

Sus manifestos pamfletarios no fueran transmitidos en primera mano a los responsables por la salud de las mujeres. Al revés, los comunicaran a la prensa que los acceptó erroneamente como verdaderos y los publico en titulos de caja alta!

Asi lograran crear el panico en las poblaciones, y la confusión de riesgos relativos con riesgos absolutos!

Títulos errados…

Los terroristas, en su manifesto escriben "estrogen" quando se refieren a estrógenos equinos conjugados, y "progestin" en lugar the MPA, un grave error permitido por los "referees" de JAMA!

Contradicciónes…

En el texto de su manifesto, en *"RESULTADOS"* dicen que sus datos no son estatisticamente significativos (!...) pero en *"DISCUSIÓN"* afirman que son clinicamente relevantes … (?!)

Exprimen sus resultados en “mujeres-año” que es un *ser* que jamás se há visto en una consulta…

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*

?

El Indice-Global…

Traducen sus resultados en terminos de un "Indice-global" una vez que tienen la noción de que su muestra no tiene el peso suficiente para que puedan hablar de cancer de mama, enfermedades CV, etc.

Pero, hasta la fecha, *no hay ningun tratado de Medicina Interna que se refiera ò describa una enfermedad designada por "indice-global"…*

WHI Hormone Program Global Index

- Designed to summarize important aspects of health benefits versus risks to facilitate monitoring by the Data and Safety Monitoring Board (DSMB).
- Defined for each woman as the earliest occurrence of CHD, invasive breast cancer, stroke, PE, endometrial cancer, colorectal cancer, hip fracture or death from other causes
- Monitoring boundaries set for CHD (for benefit) and breast cancer (for harm)
- WHI Hormone Program Trials were not powered to assess the influence of hormone use on individual components of the Global Index

Como combater el terrorismo hormonal?

El terrorismo se combate:

- con el desarrollo,

- con la información y

- con la lucha contra la desinformación

La mejor estrategia…

La estrategia mas importante es la lucha contra el no saber leer !

Tenemos que enseñar a las gentes (*mujeres y medicos*) como leer la epidemiologia !

Sin saber leer no hay información fidedigna.

Enseñar a leer
la epidemiologia…

Como se hace la epidemiologia?

Que lenguaje utiliza para se comunicar?

Vivimos hoy en la moda de la Medicina Basada en la Evidencia.

Y vivimos tambien en la moda de lo que es nuevo…

"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)

Como contrapunto de la

Medicina Basada en la Evidencia…

propongo la

Evidencia *Basada en la Medicina* !

Ò aun mejor…

La Medicina *Basada en la Inteligencia* !

(Lucas Viana Machado)

La Validez…

Los multiplos concensos publicados por Sociedade de Menopausia nacionales, regionales (EMAS, NAMS, etc) y internacionales (IMS) tienen en comum no acceptaren como norma de buena practica clinica las conclusiones del HERS, WHI y MWS por, apesar de su validez interna, no teneren validez externa!

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 interprete them?

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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 ?...

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 occuring 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**

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 statiscally significant

Does

“Statistically Significant”

always equate to

“Clinically Relevant”?

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

p Value

Is the *probability* of obtaining the observed relative risk by chance

(*p* must be < 0.05)

Type of association

- Spurious
- Indirect
- Causal
    - Strenght 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

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

El Cancer de Mama

El riesgo de cancer de mama con los E+P combinados continuos es minimo.

Se necessita tratar 1250 mujeres (NNH) durante 1 año hasta que se diagnostique 1 cancer de mama (lo que es equivaliente a el riesgo relativo de 23%!)

"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

Estrógenos aislados…

El uso de estrógenos aislados no esta asociado a un aumento de cancer de mama, lo que habia sido sugerido por los tratamientos hormonales en sobrevivientes de cancer mamario ò en las embarazadas que han tenido cancer.

Su sobrevivencia es mayor que la de los testigos y sus recorrencias y mortalidad son menores

“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

No hay mejor tratamiento para los sintomas del climaterio que los tratamientos hormonales!

SOCIEDADE PORTUGUESA de menopausa

3rd International Symposium
of the
Portuguese Menopause Society
In Celebration of the World Menopause Day

Menopause 2004

The Transatlantic Controversies - The State of the Art

October 23, 2004 *Fundação Engº António Almeida* *Oporto – Portugal*




Organizado

con *harto pino !*

The USA Vision

Chair: *M.Neves-e-Castro and Mario de Sousa*

09.00-09.30 –**Controversies about HRT – Lessons from Monkey Models**
Th.Clarkson, Wake Forest Univ.

09.30-10.00 – **Appropriate Use of Hormones Should Alleviate Concerns Regarding CV and Breast Cancer Risks**
R.Lobo, Columbia Univ

10.00-10.30 –**Implications of clinical trials for CVD in younger women**
Jacques Rossouw, NIH/NHLBI/WHI

10.30-11.00 ***Coffee Break***

11.00-11.30 – **Menopausal Therapy and Cancer Risk in the WHI**
R.Chlebowski, WHI

11.30-12.00 - **The state of the Art in the USA**
L.Speroff,Portland.Or

12.00-13.00 **- Debate and Discussion**
Chair: *J.Stevenson (UK) and S. Palacios (Sp)*

The U.S.A. “team”

1. R. Chlebowski, 2. J.Rossow, 3. R. Lobo, 4. T.Clarkson

The European Vision

Chair: *Mario de Sousa and M. Neves-e-Castro*

14.30-15.00 – **WHI and Cardioprotection: Looking Beyond the Figures**
A.Pines, Il

15.00-15.30 – **Hormone Therapy and Breast Cancer: What is the Problem?**
P.Kenemans,Nl

15.30-16.00 – **Do Estrogens Really Increase Breast Cancer Risk?**
H. Kuhl, D

16.00-16.30 –***Coffee Break***

16.30-17.00 **Strategy in Osteoporosis Management Following WHI**
D.Barlow, UK

17.00-18.00 **Debate and Discussion**
Chair:*A. Genazzani (I) and J.Calaf (Sp)*

18.00 **-** **Conclusions**
M.Neves-e-Castro

The European “team”

1. D.Barlow, 2. H. Kuhl, 3.P.Kenemans, 4. A.Pines

Conclusions of the

3rd International Symposium Menopause 2004, the State of the Art and the Transatlantic Controversies

by

Manuel Neves-e-Castro

Chairman of the Symposium

Portuguese Menopause Society

Porto, October 23, 2004

The conclusions of this 3rd International Symposium of the Portuguese Menopause Society reflect not only what the speakers have said but, may be even more important, *how it applies to clinical practice.*

Many position statements have been issued by National (PMS), Regional (EMAS, NAMS) and International Societies (IMS) all having in common a strong disbelief in the external validity of the epidemiological studies like HERS, WHI, Million Women Study

PMS www.spmenopausa.pt

EMAS www.emasonline.org

NAMS www.menopause.org

IMS www.imsociety.org

We believe that as to CHD, both the primate studies and clinical evidence suggest strongly that HT can be preventive if started very early after the menopause, preferably after a regimen of oral contraceptives given during the perimenopausal years

Clarkson TB. *Fertil Steril* 2004;81:1498-1501
Grodstein F et al. *N Engl J Med* 2000;343:530-537
Stampfer MJ. *NAMS 2004*;PS#2
Victory R et al. *Fertil Steril* 2004;82:O-130

In regard to breast cancer, we may accept in E+P treatments a very slight increase in the number of diagnosed cancers that is *irrelevant in clinical practice in view of how we medicate and follow our patients.*

However, the E only arm of WHI strongly suggests that an estrogen only medication is not only *devoid of risk but may even be protective.*

This is supported by previous investigations of pregnancy following breast cancer or HT in breast cancer survivors.

Gelber s et al. *J Clin Oncol* 2001;19:1671-1675
WHI Group *J Am Med Assoc* 2004;291:1701-1712
O'Meara et al. *J N C I* 2001
DiSaia et al. *Am J Clin Oncol 2000*
Nananda F Col et *al.J Clin Oncol;2001*:19:2357-2363

Recent reports did not find, for continuous combined treatments, any increased risk of either CHD or breast cancer.

The difference from WHI being that women were younger, symptomatic and with lower body weights

Heikkinen J. *NAMS* 2004, Abstract LB38
Lobo R. *Arch Int Med 2004;164:482-484*

We are impressed with reports from Australia that strongly suggest that the addition of testosterone to continuous combined regimens does not show their increased risk of breast cancer compared with controls *(a finding that may favor the use of tibolone).*

Dimitrakakis C et al. *Menopause* 2004;11:531-535

Recent observations also suggest that the addition of Omega 3 fatty acids added to the diet as well as low dose aspirin offer a good protection against breast cancer in women under hormonal treatments

Sadeen P et al. *Obstet Gynecol Survey* 2004;59:722-730

Terry MB et al. *J Am Med Assoc* 2004;291:2433-2440

Ideally,HT should use estradiol
(*preferably by a parenteral route*)
added to natural progesterone
***by the vaginal route*,**
or to a *medicated IUD* (Mirena**)**

The Portuguese Menopause Society, on the basis of this important Symposium and of recent published data, again sees no reason to suggest any major modification in the adopted rules of good clinical practice

We think that the major indication of HT in the menopause is for symptom relief and quality of life.

However, we do not discard the possibility of its primary prevention effect when given soon after the menopause particularly in terms of *CVD, osteoporosis and colon cancer*

We reemphasize the need to implement very important collateral measures, like

- normalization of body weight,

- abstention from tobacco,

- low alcohol consumption,

- exercise,

- Mediterranean diet,

etc .

Obesity and a late first full term pregnancy are, among others, *preventable risks factors for breast* cancer that are more important than HT's in general.

Kuhl H. *J Am Med Assoc* 2004;292:683

In so doing we repeat the *definition* of the safe woman to start HT based on the conclusions of the previously mentioned studies:

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. Human Reproduction 2003;18:2512-2518

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. Human Reproduction 2003;18:2512-2518

If there are no incoming contraindications we see no reason to establish a time limit to the duration of therapy, mainly if there is a recovery of symptoms after its discontinuation

Cochrane B, *NAMS 2004*, P53

IMS www.imsociety.org

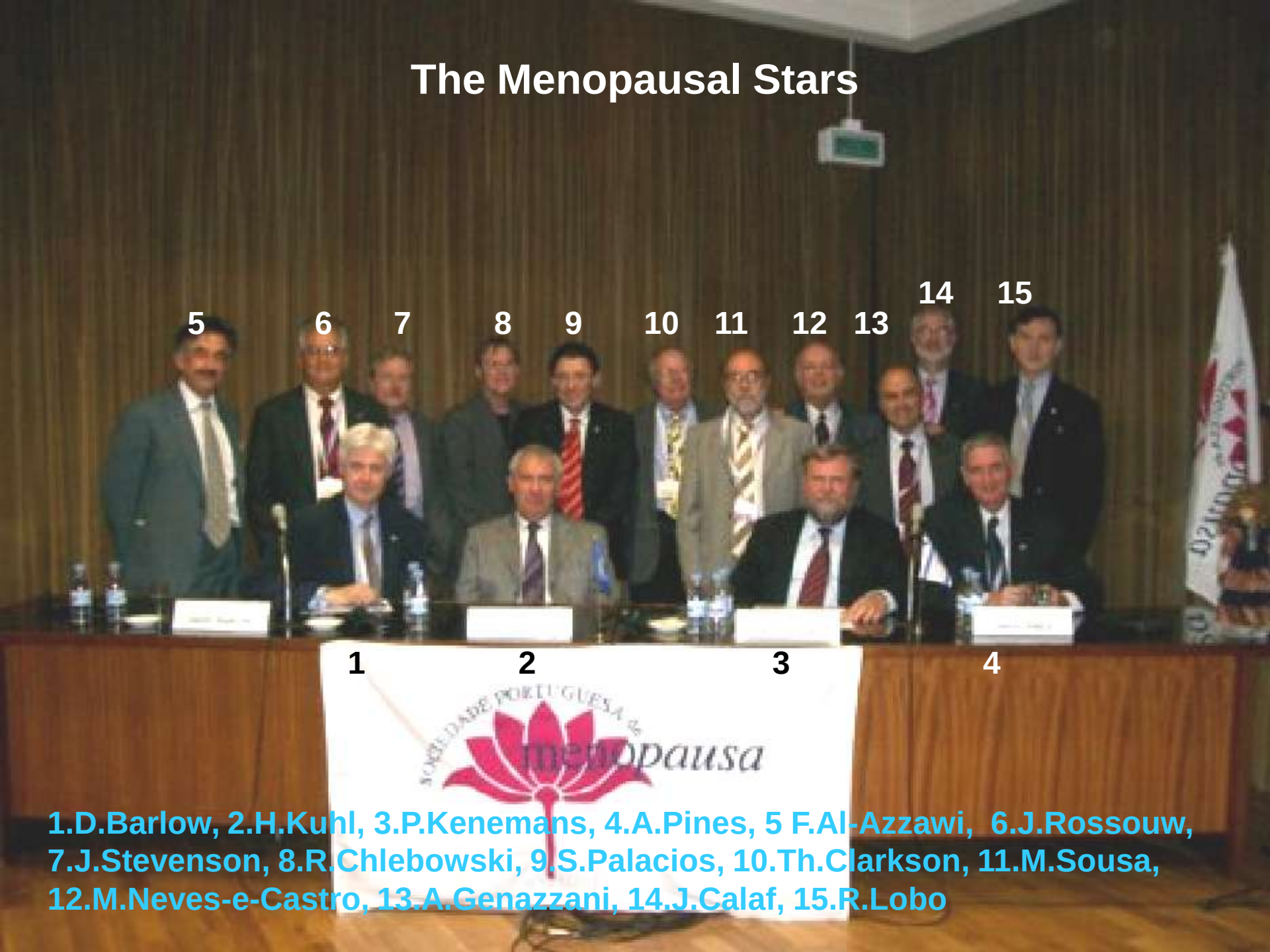
NAMS www.menopause.org

In conclusion ,and in the light of present evidence,

doctors and women should be reassured that the suggested HT's for the relief of symptoms in the menopause

are safe and very effective

The Menopausal Stars



1.D.Barlow, 2.H.Kuhl, 3.P.Kenemans, 4.A.Pines, 5 F.Al-Azzawi, 6.J.Rossouw, 7.J.Stevenson, 8.R.Chlebowski, 9.S.Palacios, 10.Th.Clarkson, 11.M.Sousa, 12.M.Neves-e-Castro, 13.A.Genazzani, 14.J.Calaf, 15.R.Lobo

Epidemiological Studies

PLEASE!

Do not read only the tittles…

Do not read only the abstracts…

Do read the full paper !

Be critical!

Make up your own mind!

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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

Dijo ***zamba*** y ***canuta !***

Muchas gracias !