



Joint Aches and Pain: Individualizing therapy for climacteric symptoms

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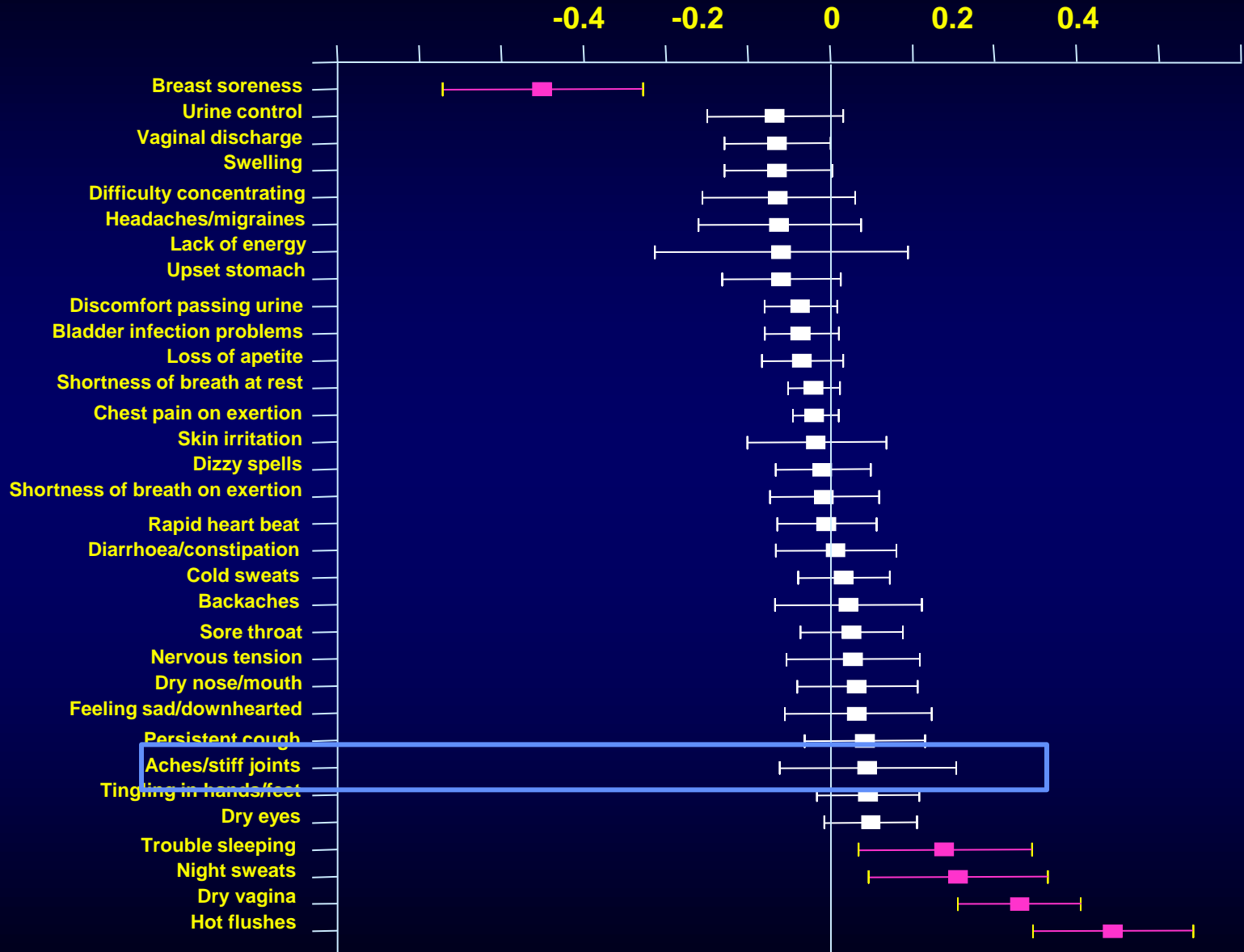
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Aches and joint pain

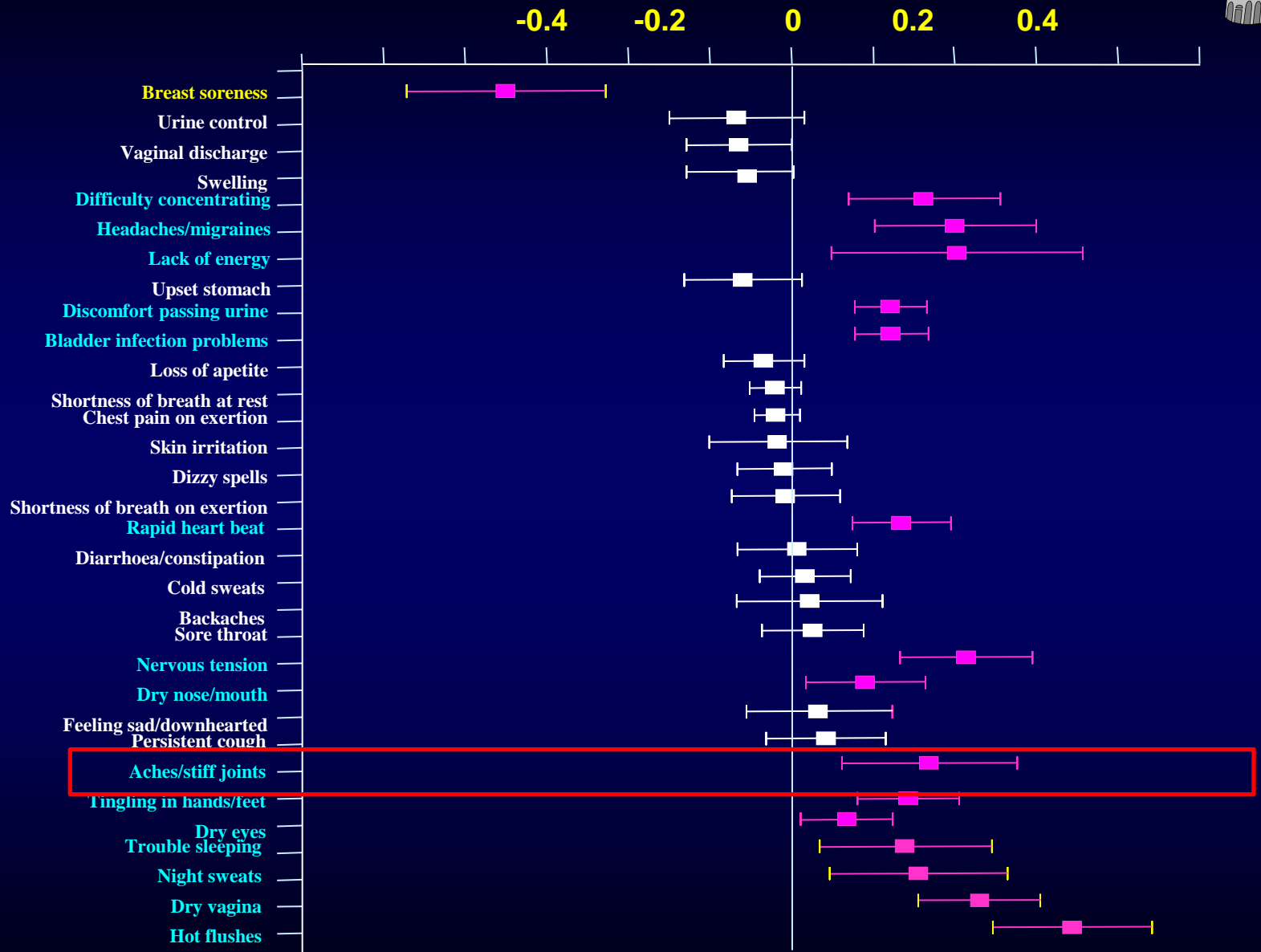
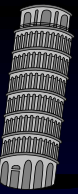
- Are these symptoms related to menopause/estrogen decline ?
 - Are these symptoms related to CNS effects of estrogen deficiency ?
 - Are these symptoms linked to local effects of estrogen deficiency?

 - Can HRT decrease /avoid / eliminate the symptoms ?
-

CHANGE IN SYMPTOM SCORES: PRE&EARLY PERI VERSUS LATE PERI & POST



CHANGES IN SYMPTOM SCORES IN 1125 PMW PRE VERSUS POST



Aches and joint pain

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EFFECTS OF SEX STEROIDS ON CNS

- NEURONAL EXCITABILITY
 - NEUROPROTECTION
 - COGNITIVE FUNCTIONS
 - MOTOR COORDINATION
 - AFFECTIVE STATE
 - MOOD
 - LIBIDO
 - SLEEP
 - **PAIN THRESHOLD**
-

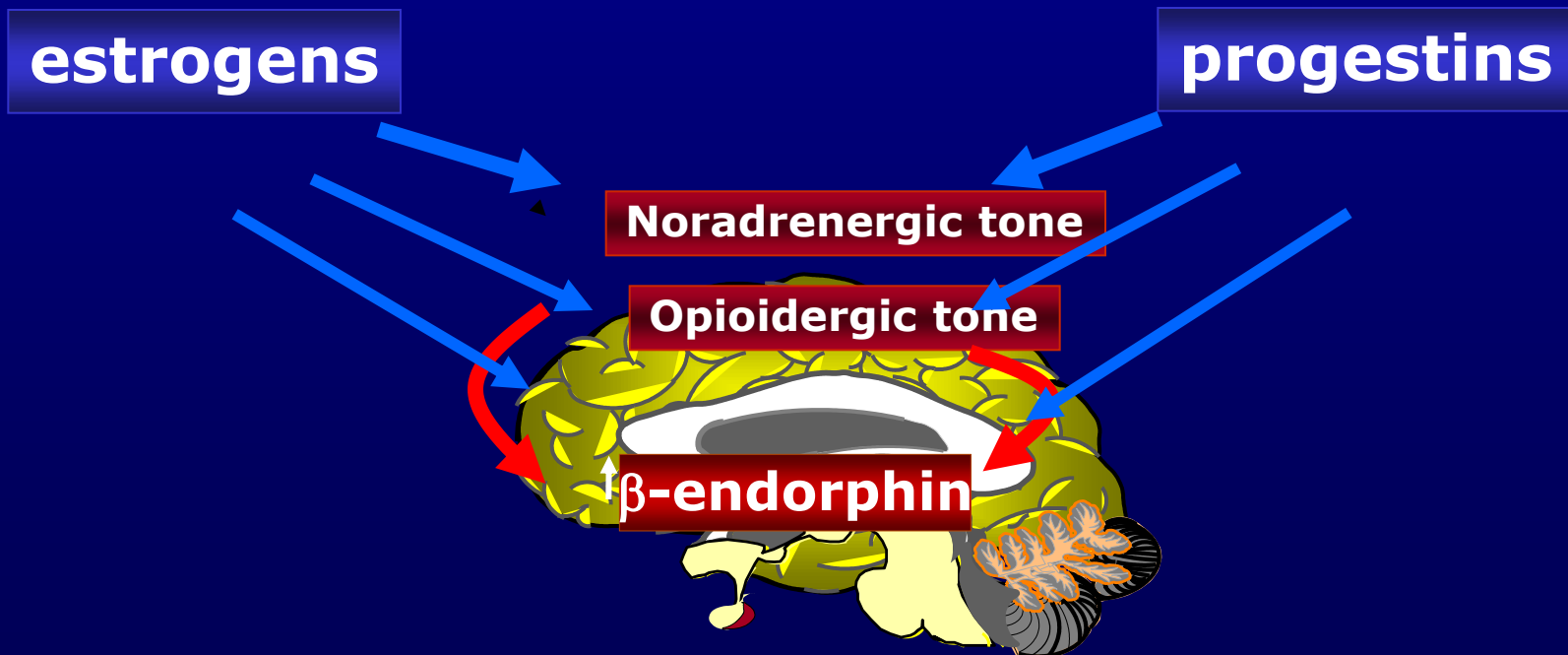
Aches and joint pain

- Are these symptoms related to menopause/estrogen decline ?
 - Are these symptoms related to CNS effects of estrogen deficiency ?
 - The estrogen deficiency can decrease the pain threshold
 - The sudden onset of pain suggests an involvement of CNS
-

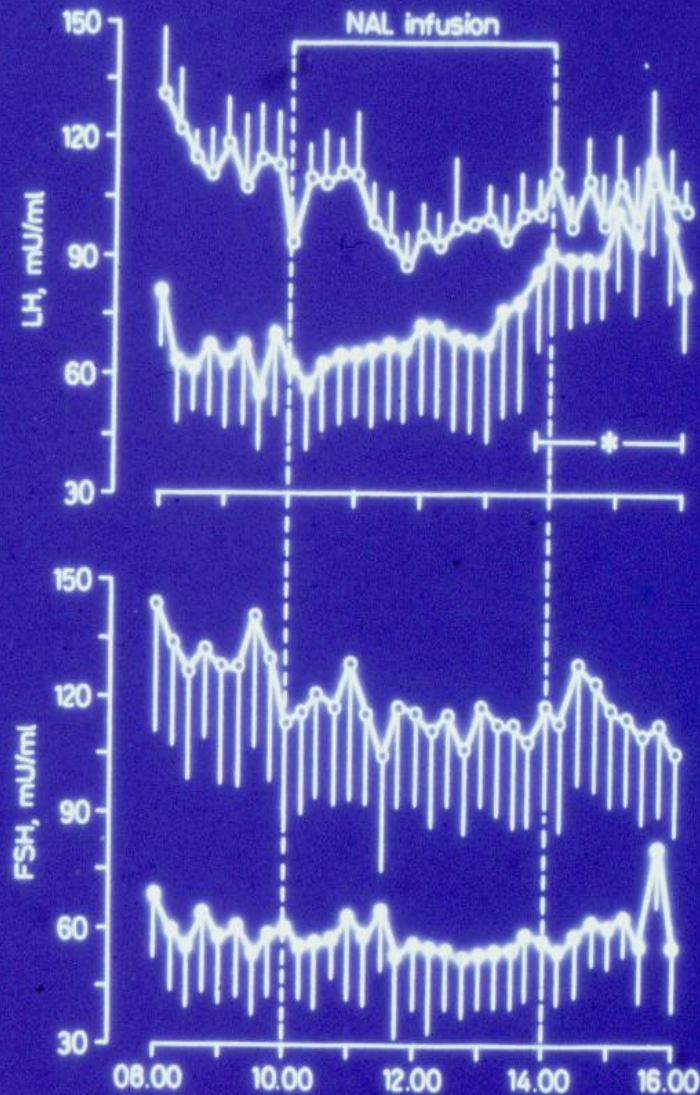
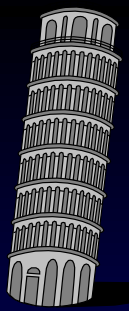
brain function and menopause

Postmenopause is associated with a

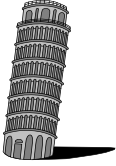
- reduction of β -endorphin production in the CNS
- decreased peripheral β -endorphin levels
- lack of plasma β -endorphin response to clonidine or naloxone tests



NEUROENDOCRINOLOGY OF POSTMENOPAUSE

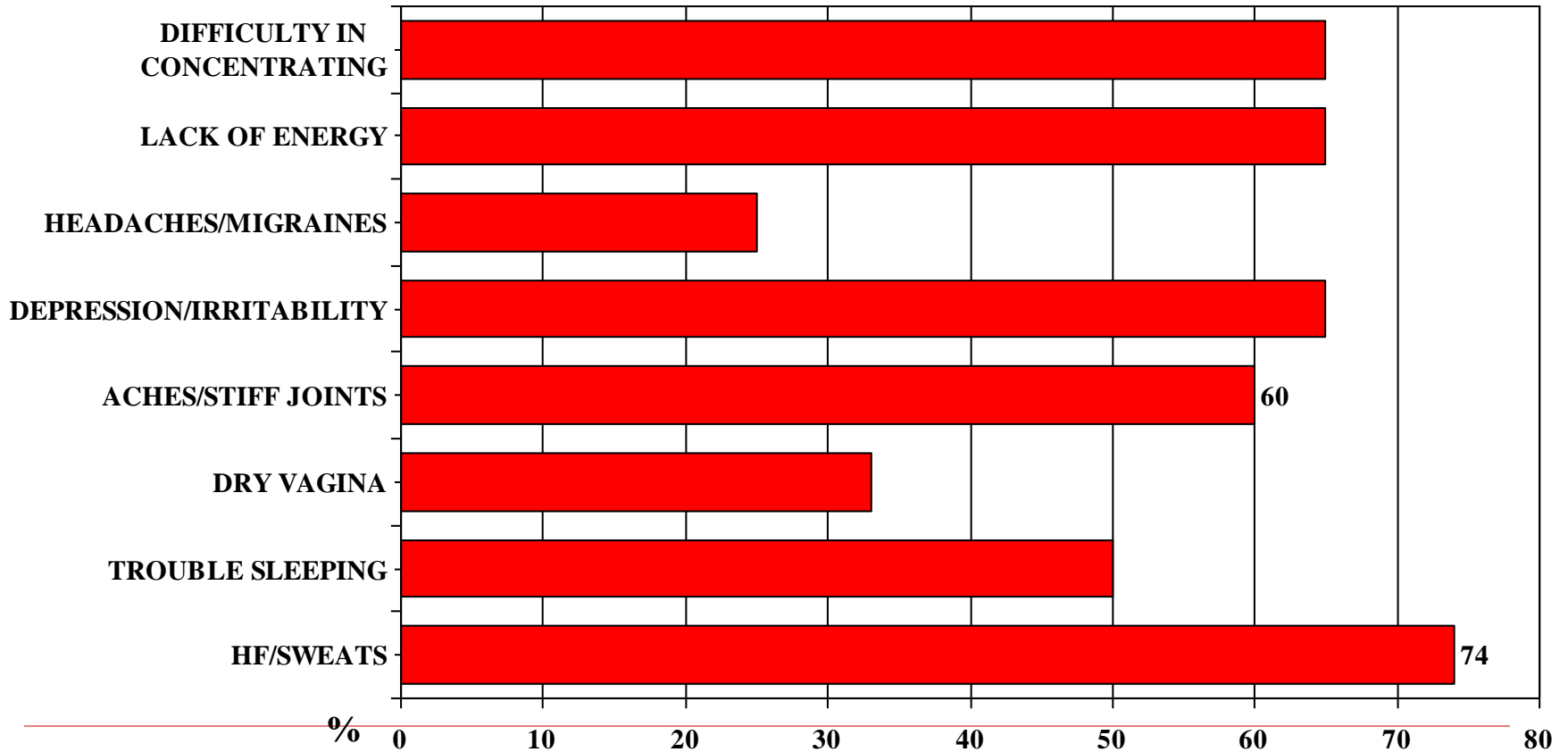


from Melis et al. Neuroendocrinology, 1984



MENOPAUSAL TRANSITION : EFFECTS ON SYMPTOMS (n=496)

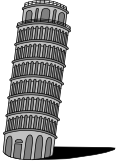
WOMEN EXPERIENCING SYMPTOMS THROUGH TRANSITION



Aches and joint pain

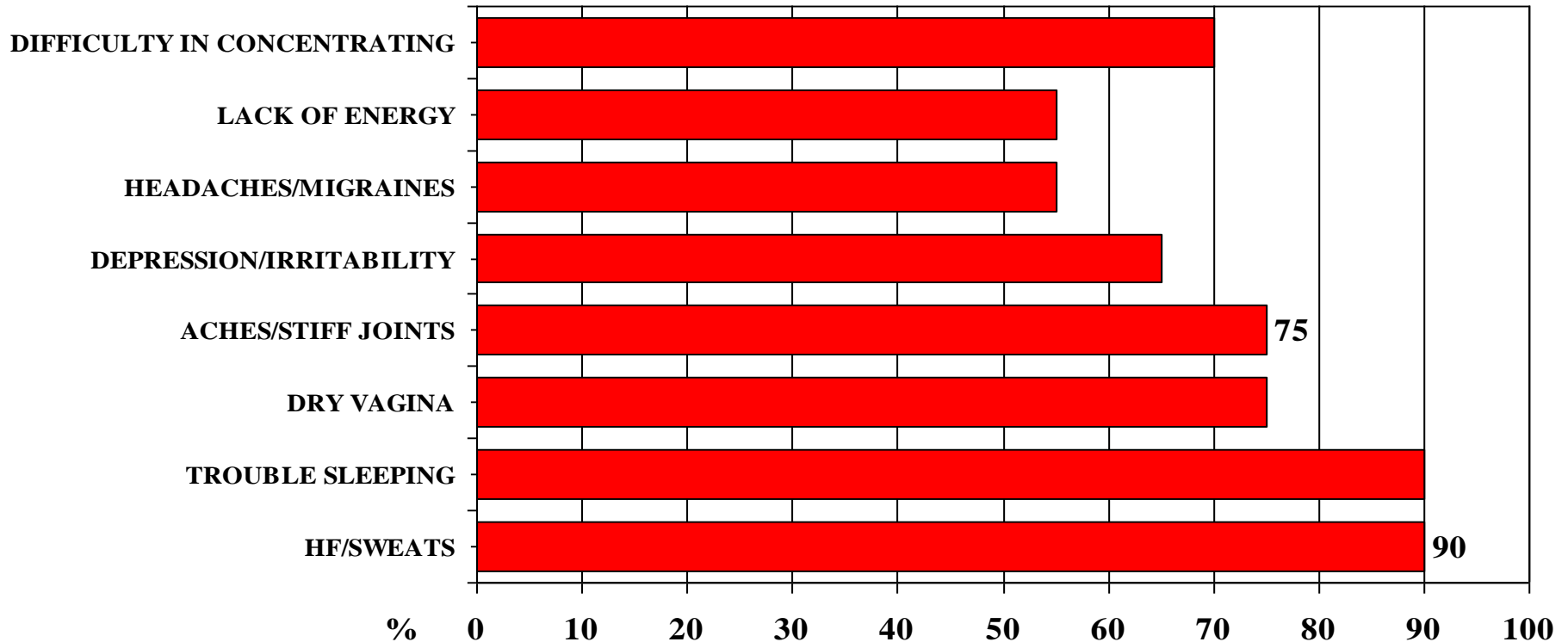
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-



MENOPAUSAL TRANSITION : EFFECTS OF LD-HRT ON SYMPTOMS AFTER 3 MONTHS (n= 95)

WOMEN EXPERIENCING IMPROVEMENT



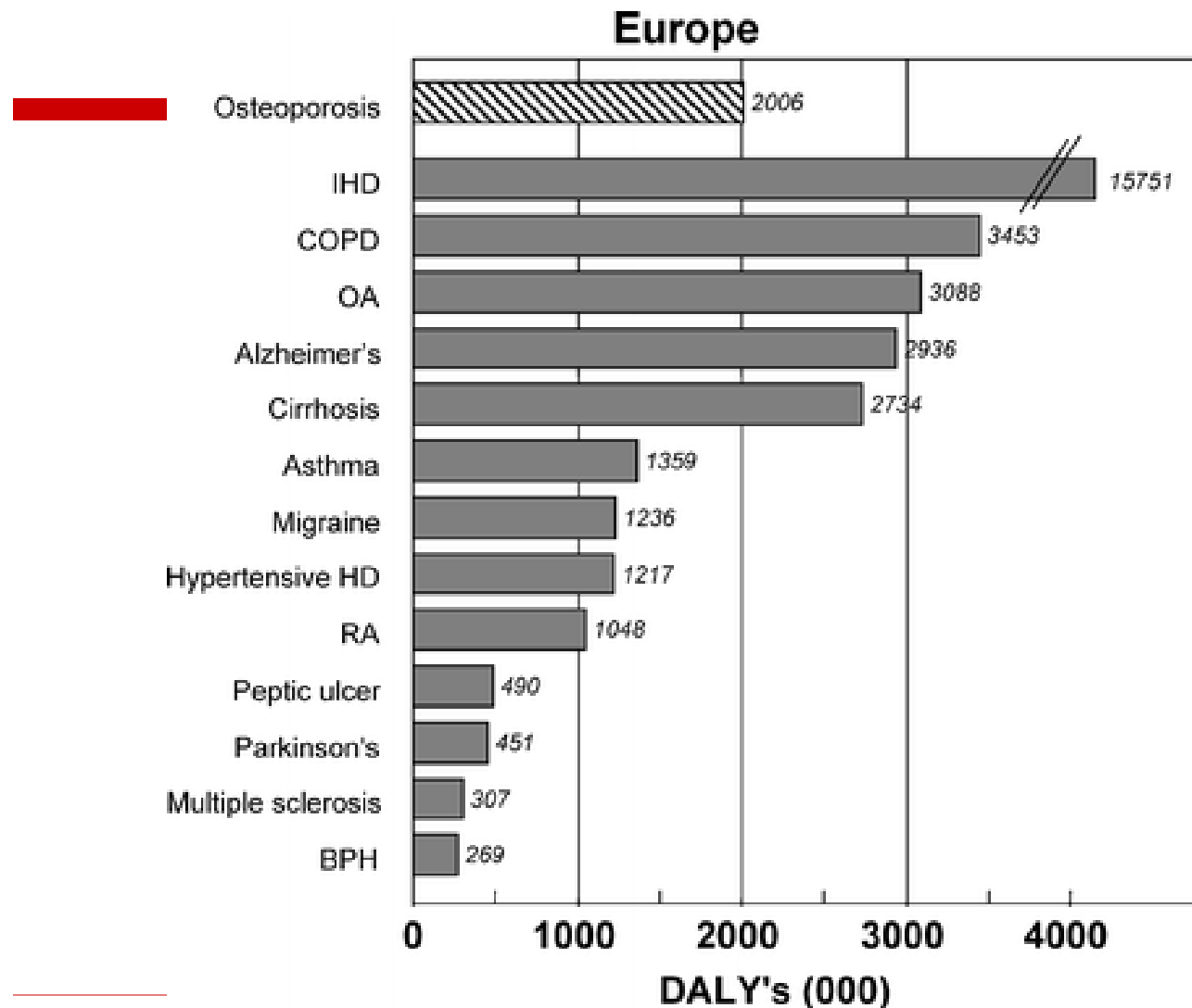
▪ *M.Gambacciani, in preparation*

Aches and joint pain

- Are these symptoms related to menopause/estrogen decline ?
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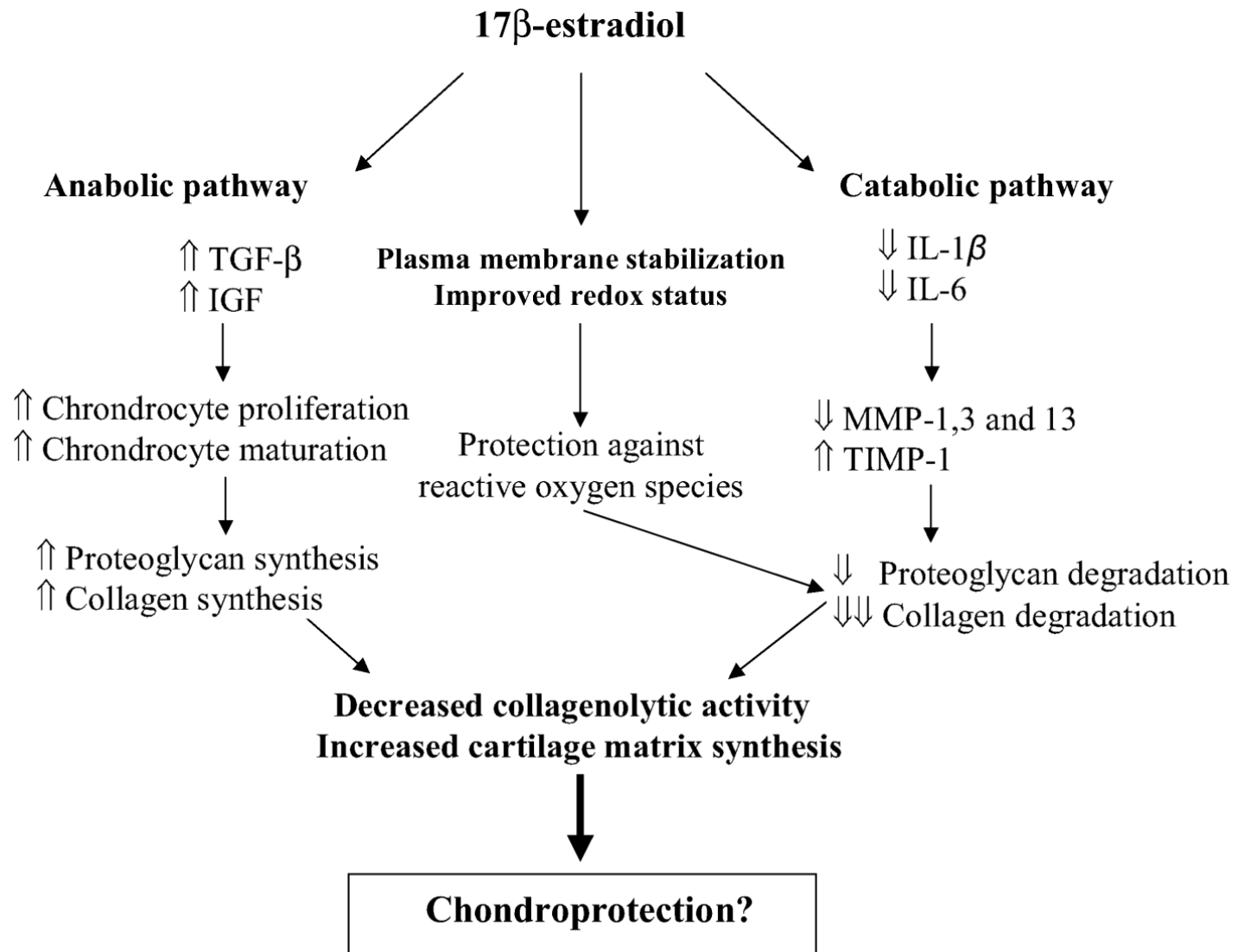
 - Can HRT decrease /avoid / eliminate the symptoms ?
-

Disability-adjusted life-years (DALYs) lost due to noncommunicable diseases in Europe



(IHD ischaemic heart disease, COPD chronic obstructive pulmonary disease
OA osteoarthritis, RA rheumatoid arthritis, BPH benign prostatic hyperplasia)

An update review of cellular mechanisms conferring the indirect and direct effects of estrogen on articular cartilage

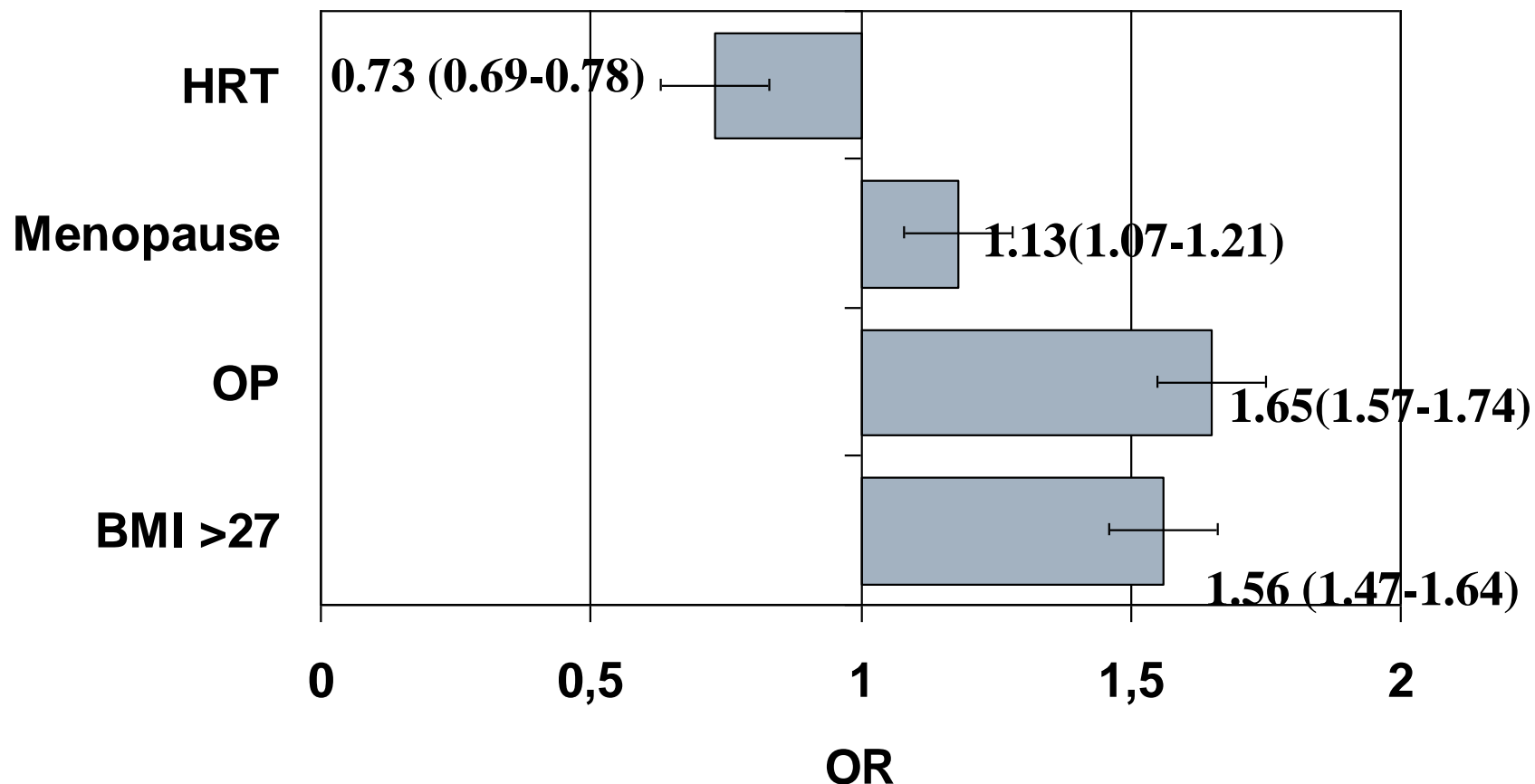


Estrogen and connective tissue

- Estrogen receptors have been identified on fibroblasts of connective tissue
 - Estrogens play a critical role in the regulation of metabolic and functional processes of connective tissue in different organs and apparatuses.
 - Modifications of estrogenic milieu interfere with the synthesis of extracellular matrix, as hydrophilic glycosaminoglycans, the water content, collagen and elastin.
-

Menopausal status, HRT and risk of osteoarthritis in women attending menopause clinics in Italy

Out of 42,464 women (mean age 53 yrs), 12,521 women reported OA.



Risk factors for osteoarthritis

Melbourne Women's Midlife Health Project

- **438 women had been followed annually over 11 years. A total of 224 of these women agreed for their knees and hands to be X-rayed in the 11th year of follow-up, and formed the final study group.**

- **significant risk factors for radiological knee OA**

- **increasing age**
- **body mass index**
- **Frequent physical activity in younger years (age 20-29 yrs)**
- **no use of hormone therapy**

ESTROGEN AND OSTEOARTHRITIS

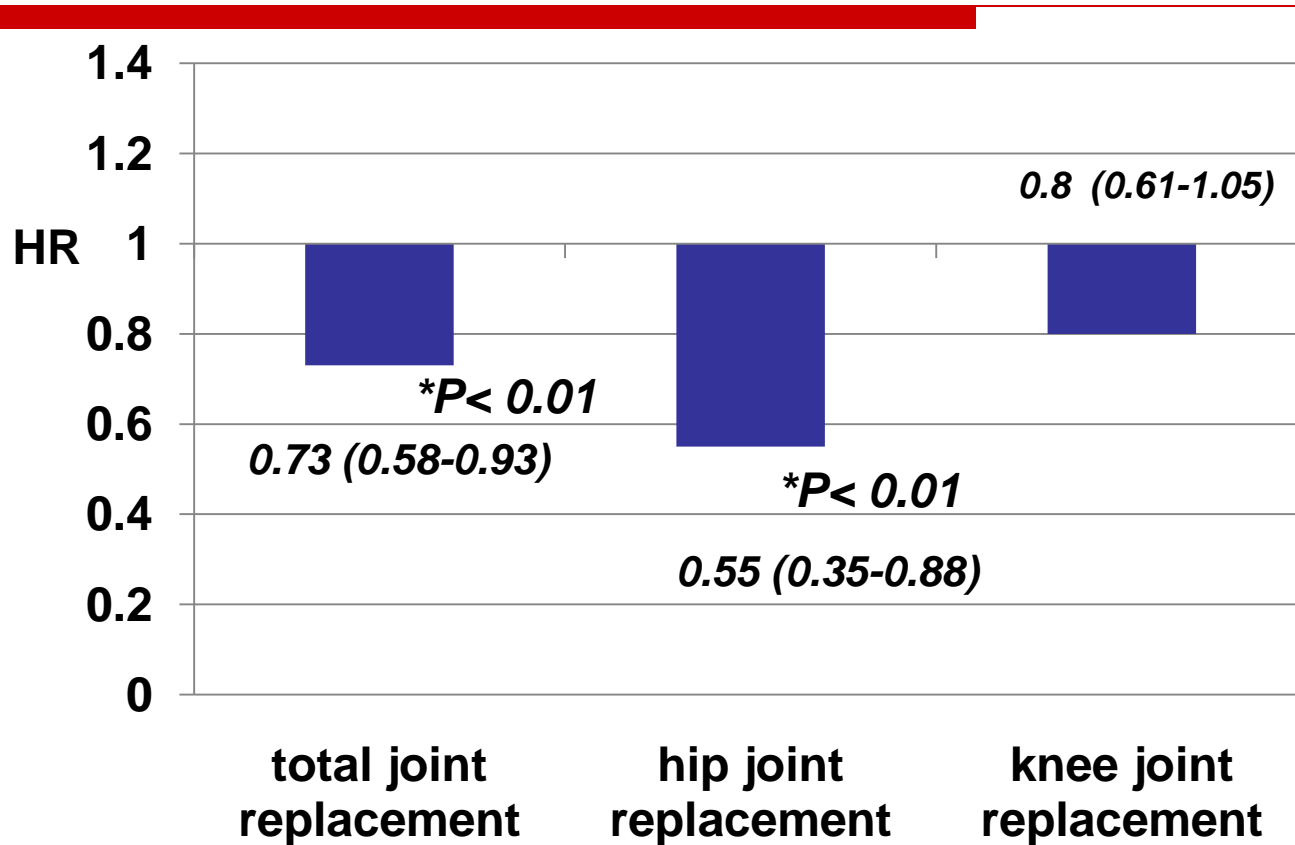
Effect of Unopposed-estrogen on risk of hip and knee joint replacement in the Women's Health Initiative

Estrogen

Placebo

N=5076

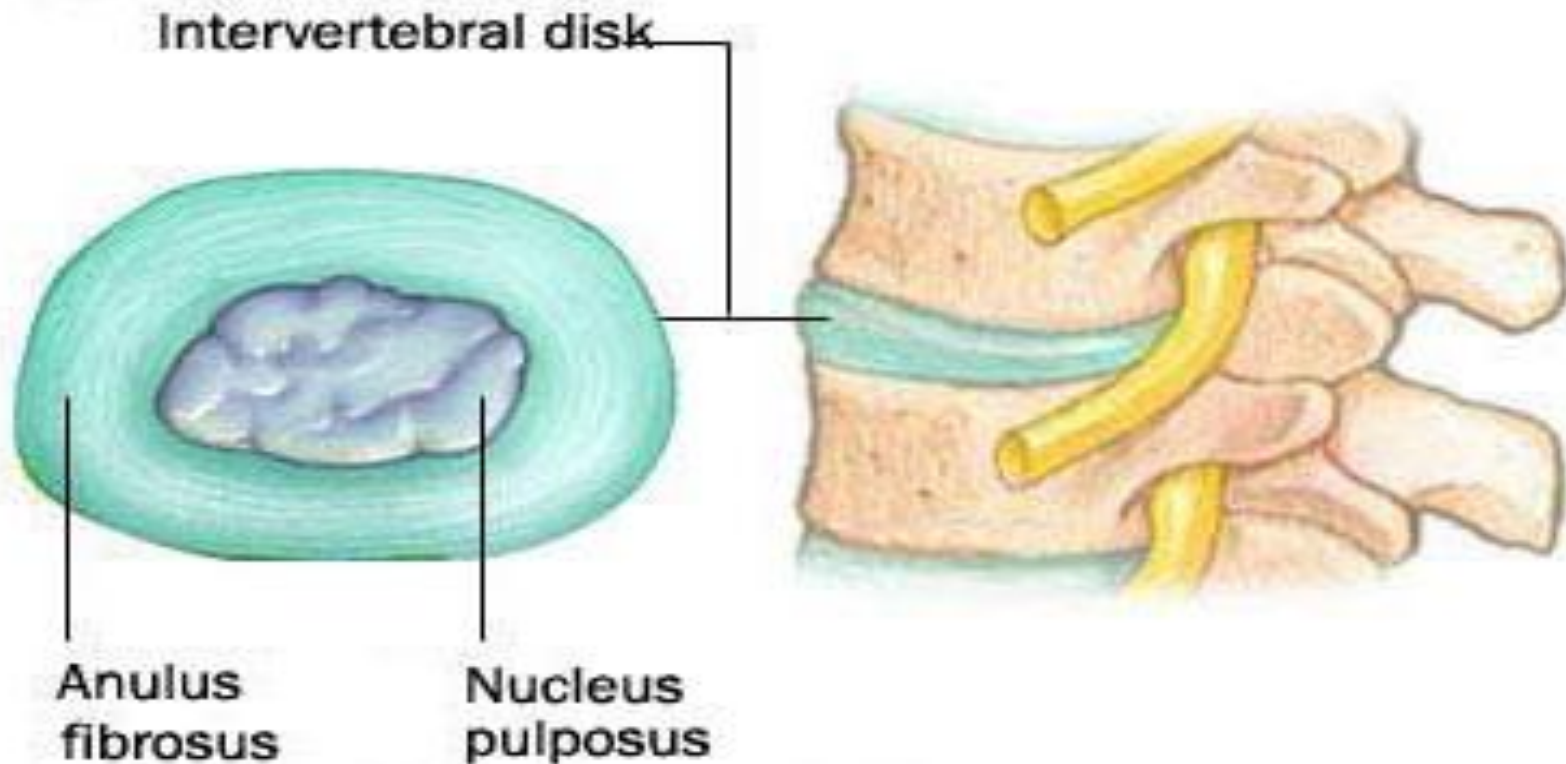
n=5196



Compliance more than 80%

Intervertebral disk: a target of hormonal action

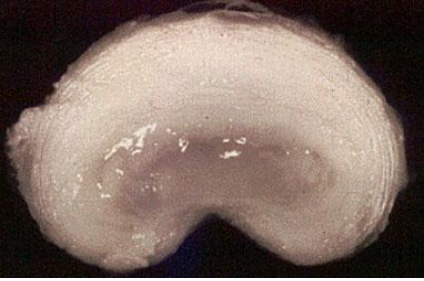
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intervertebral disk is an elastic pad of cartilage between each vertebra

The disks consist of a tough, fibrous outer covering (annulus fibrosus) and a jelly-like center (nucleus pulposus).

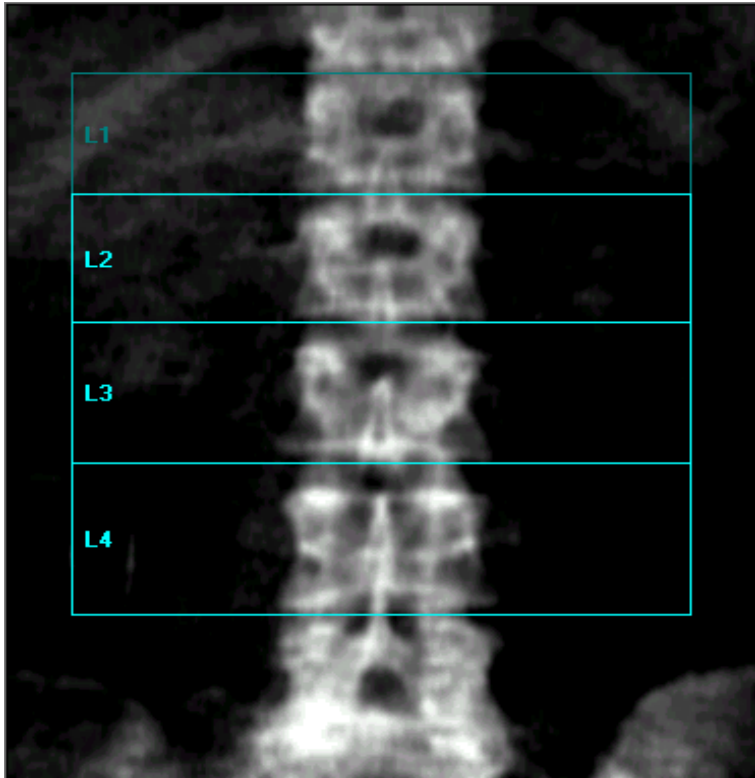


Intervertebral Disks

- The disc components, the nucleus pulposus and the annulus fibrosus, contain a balanced distribution of different collagen types, elastin, hydrophilic glycosaminoglycans and water
- Intervertebral discs are responsible for 25% of the spinal column height
- Allow spine flexibility
- Also act as “shock absorbers” of the spinal column
- This may have an impact on osteoporotic compression fracture



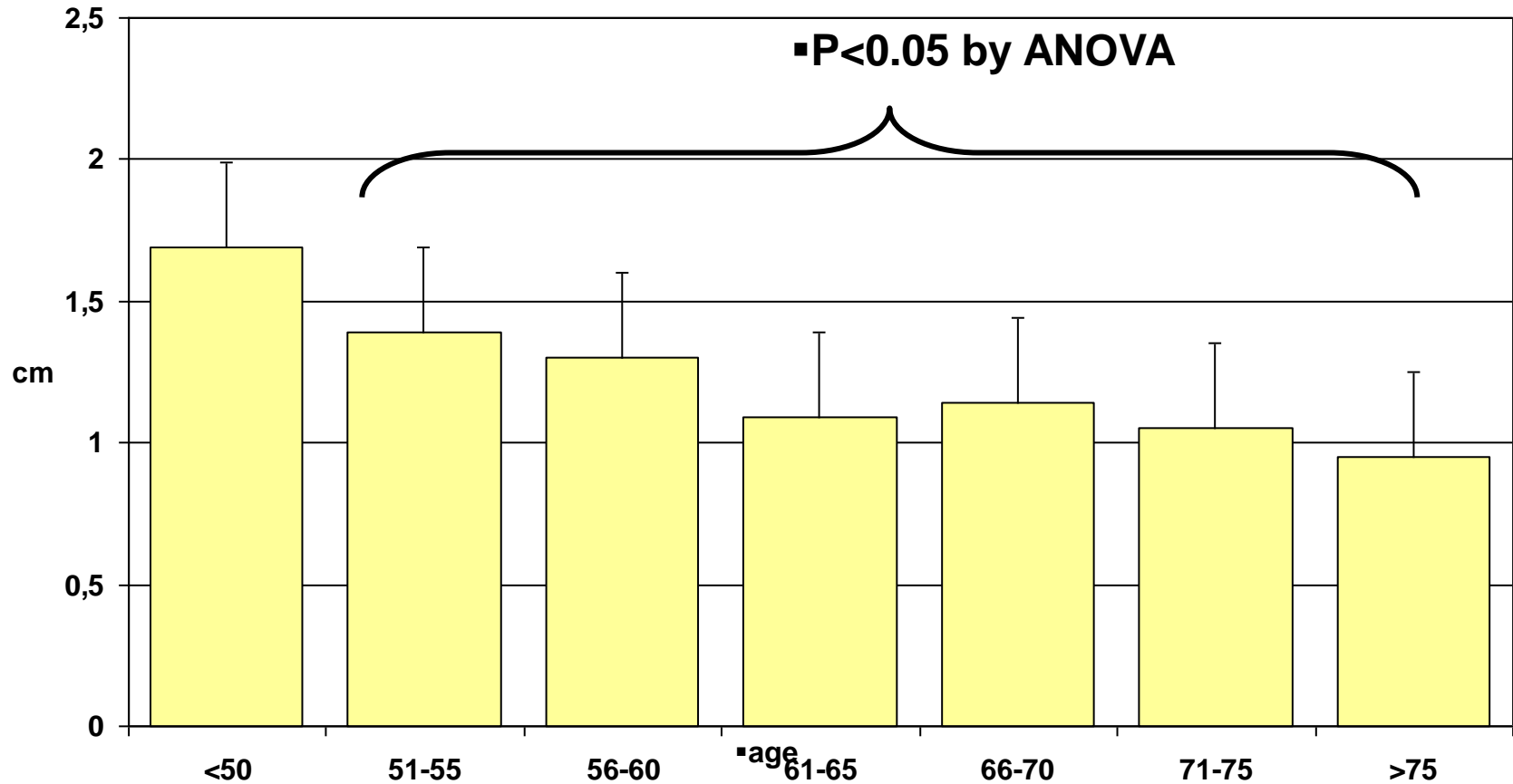
Intervertebral disc height (D1-D4) measurement



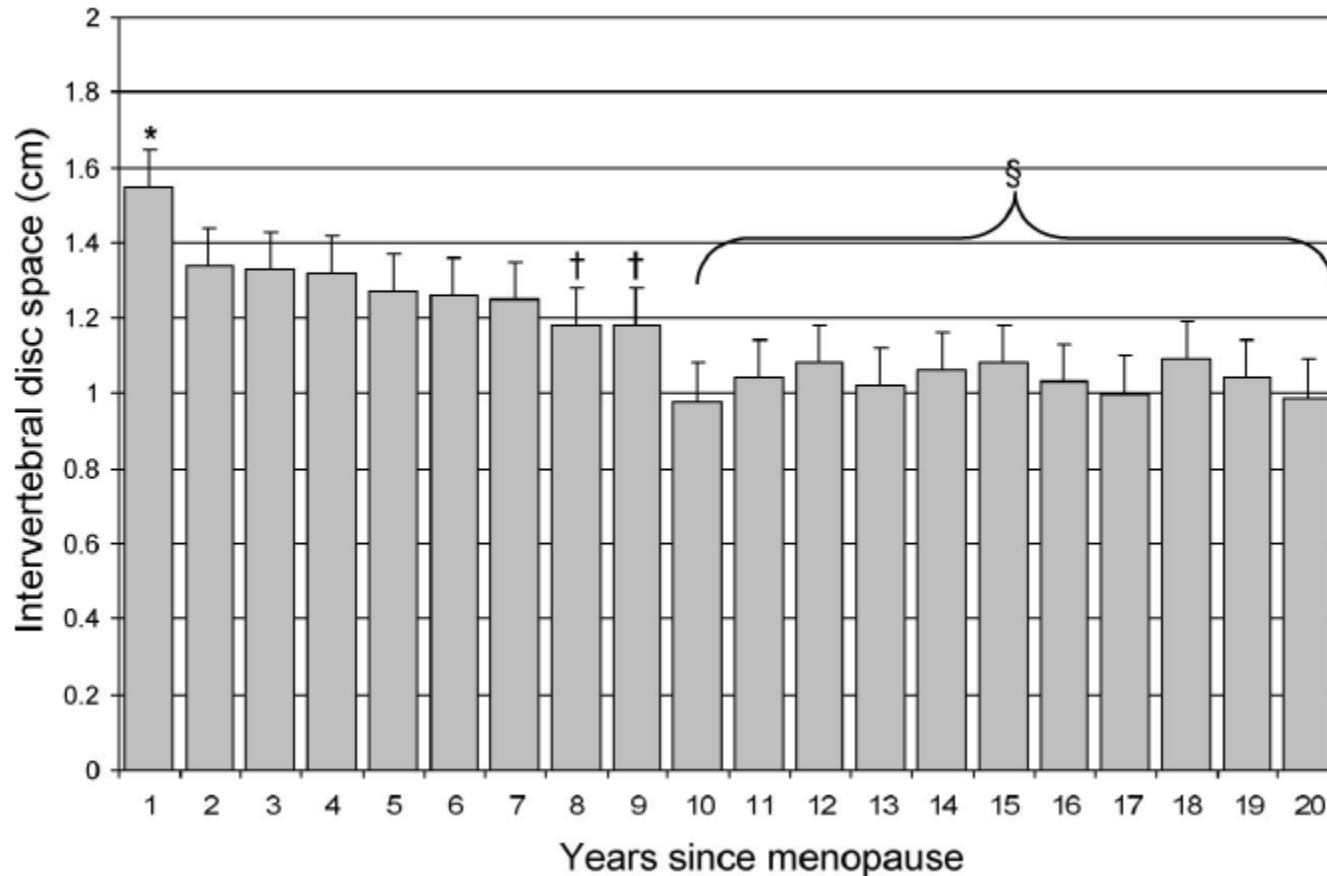
- D1: Intervertebral space between T₁₂-L₁
- D2: Intervertebral space between L₁-L₂
- D3: Intervertebral space between L₂-L₃
- D4: Intervertebral space between L₃-L₄
- D1-D4 : Intervertebral spaces between T₁₂-L₄



Intervertebral disc height (D1-D4) according to age (n=464)

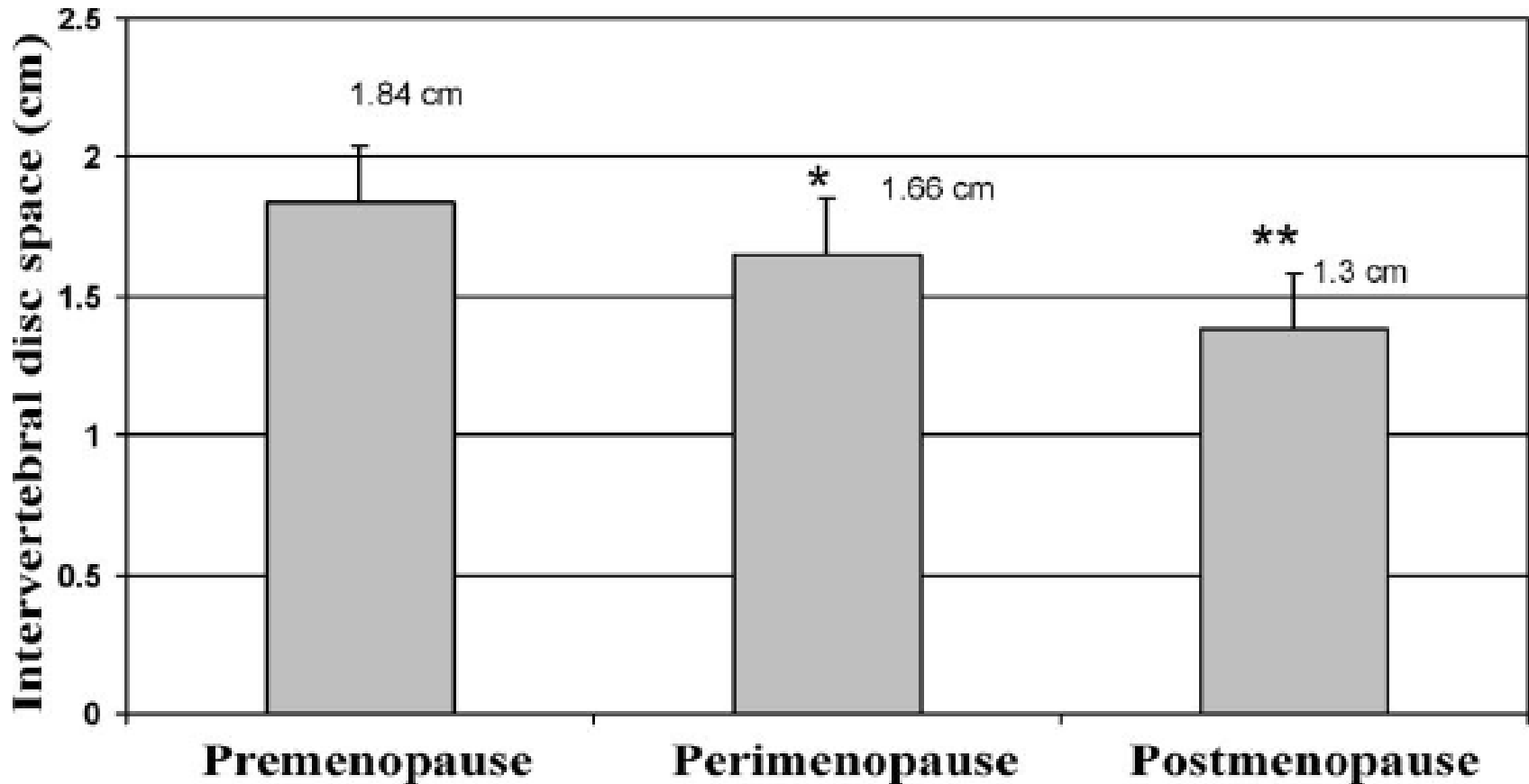


The relative contributions of menopause and aging to postmenopausal reduction in intervertebral disk height



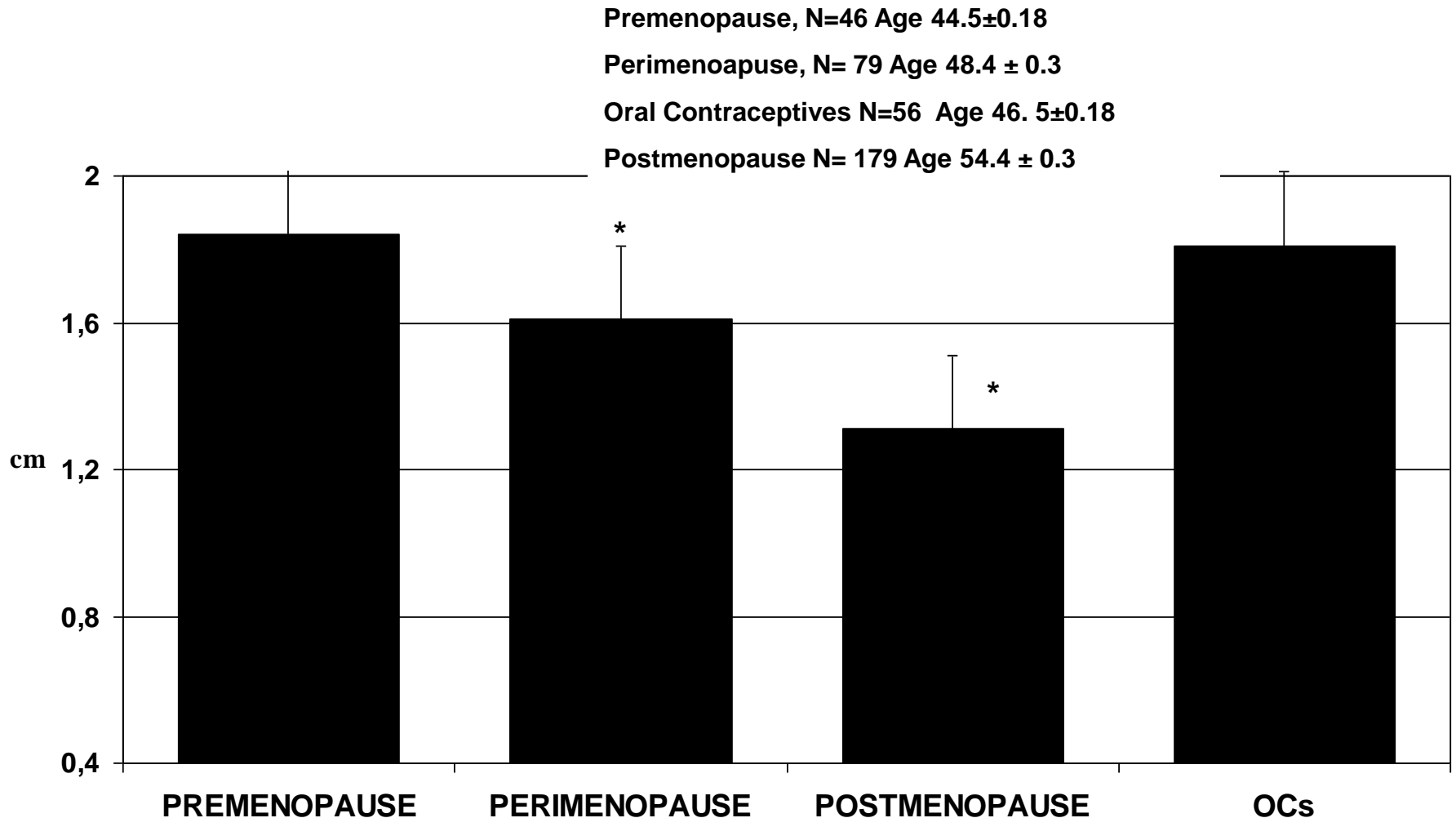
Intervertebral disc space in normal postmenopausal women (n. 312) plotted as a function of years since menopause. * $p < 0.05$ vs. other groups; { $p < 0.05$ vs. preceding groups; † $p < 0.05$ vs. preceding groups, by Fisher test

Intervertebral disc height (D1-D4) in 3 groups of age matched (47 yrs; n=39 in each group) of pre-, peri- and postmenopausal women



$p < 0.001$ by ANOVA, * $p < 0.0024$ vs premenopausal group ; ** $p < 0.0001$ vs premenopausal and perimenopausal groups.

Intervertebral disc height (D1-D4) in perimenopausal women



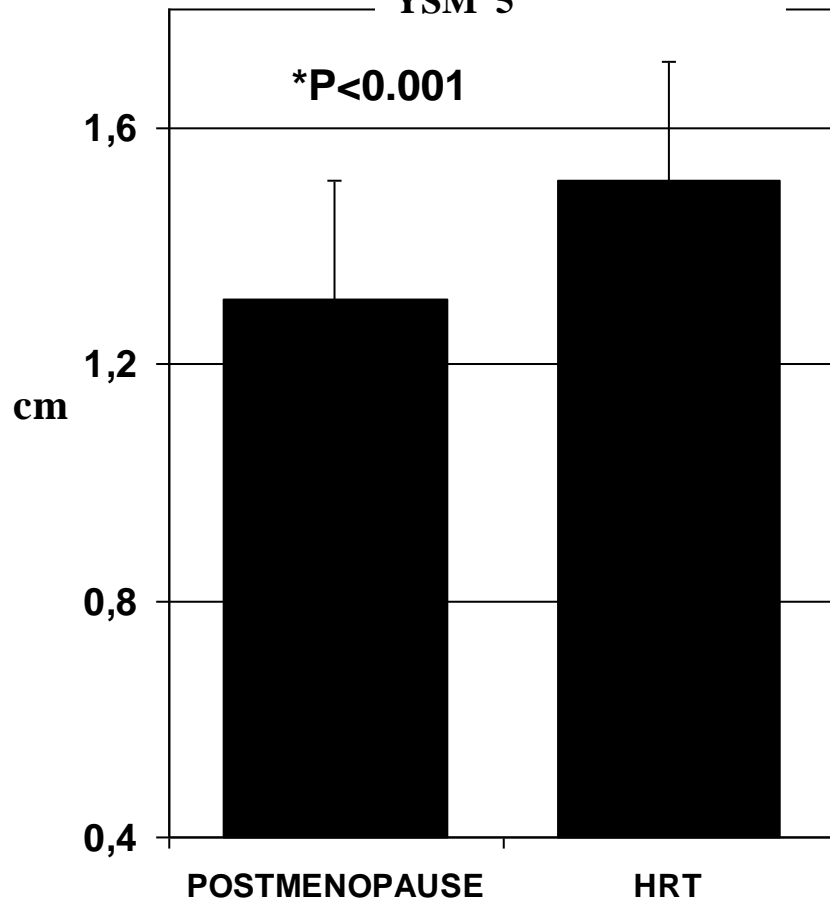
* p<0.0001 vs premenopausal group.

Intervertebral disc height (D1-D4) in postmenopausal women

N= 179

Age 54.4 ± 0.3

YSM 5

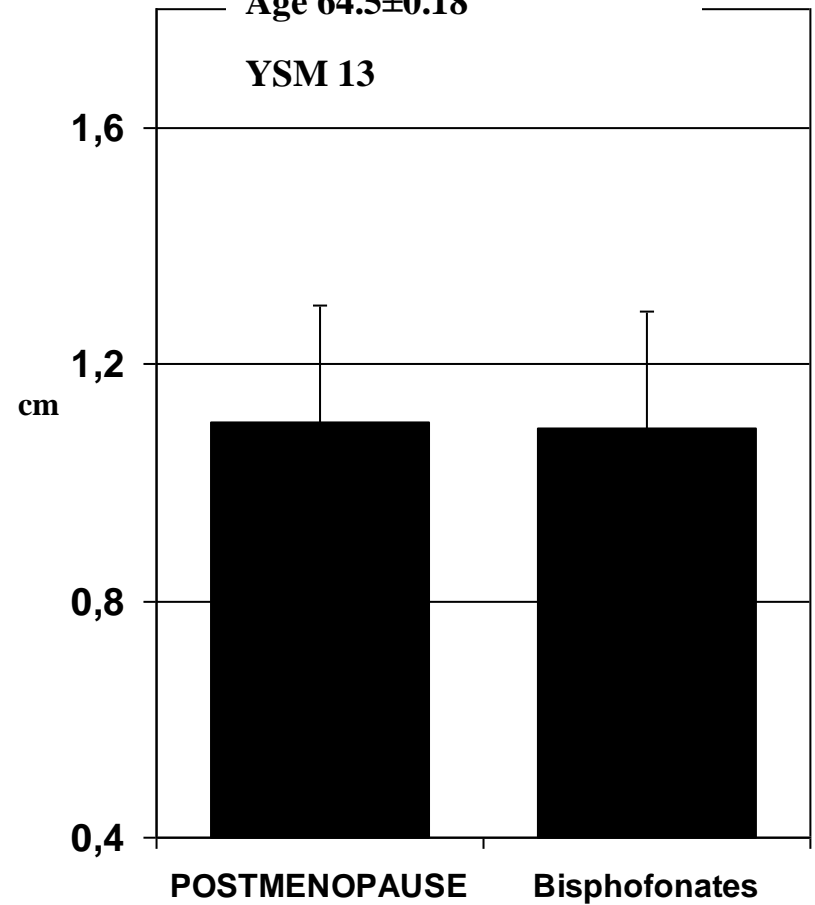


* $p < 0.0001$ vs calcium treated group.

N=46

Age 64.5 ± 0.18

YSM 13



INTERVERTEBRAL DISK HEIGHT CLIMACTERIC CHANGES

- 1. Intervertebral disc height is progressively reduced during menopause transition, independently of age**
 - 2. The decrease is more evident in the first years after menopause**
 - 3. HRT but not other antiresorptive agents, can counteract these changes**
-

Skin and connective tissue

IMS International Menopause Society

'HT has benefits for connective tissue, skin, joints and intervertebral disks.'

NAMS North American Menopause Society

No statement.

Pines A, et al, for the International Menopause Society. Press statement 27 February 2007. www.imsociety.org.

Position statement 2007 Mar. The North American Menopause Society. Menopause. 2007;14(2);168-182.

The EMAS 2008 update on clinical recommendations on postmenopausal hormone replacement therapy

- It is important to include in the evaluation of the balance between benefits and risks of HRT the increase in quality of life and climacteric symptoms.
- EMAS strongly recommend evaluating individual risks factors before prescription of an HRT.
- ...when appropriate HRT is given after an individual clinical evaluation, the benefits will far outweigh any potential risks by respecting contraindications.

