

Scuola Permanente di Perfezionamento in
Ginecologia ed Ostetricia - X EDIZIONE

LA TERAPIA ORMONALE NELLA DONNA



Direttori del Corso:
G.B. La Sala
S. Venturoli
A. Volpe

VENEZIA
ISOLA DI SAN SERVOLO

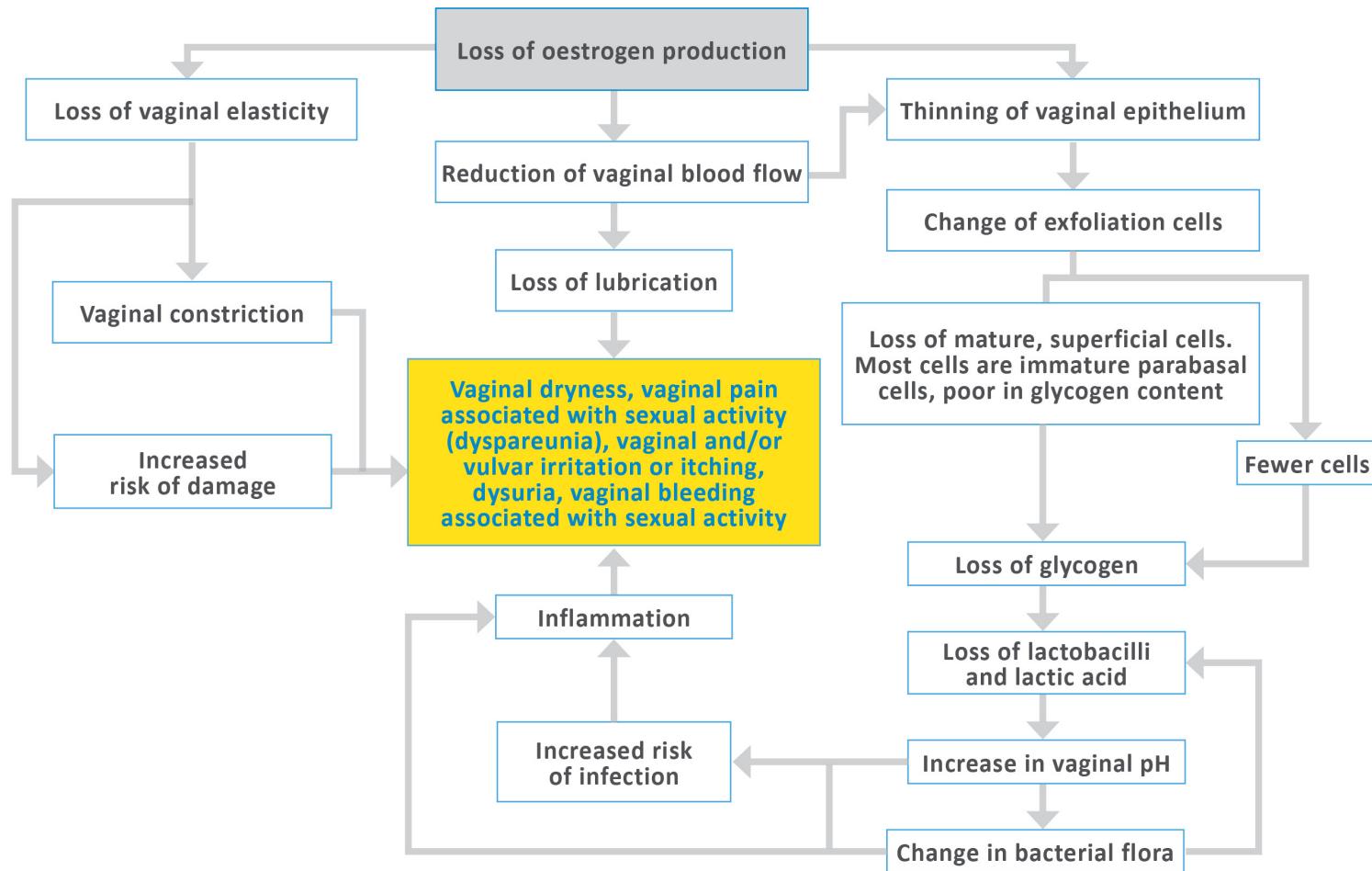
16/18 OTTOBRE 2019

RICHIESTI I CREDITI ECM

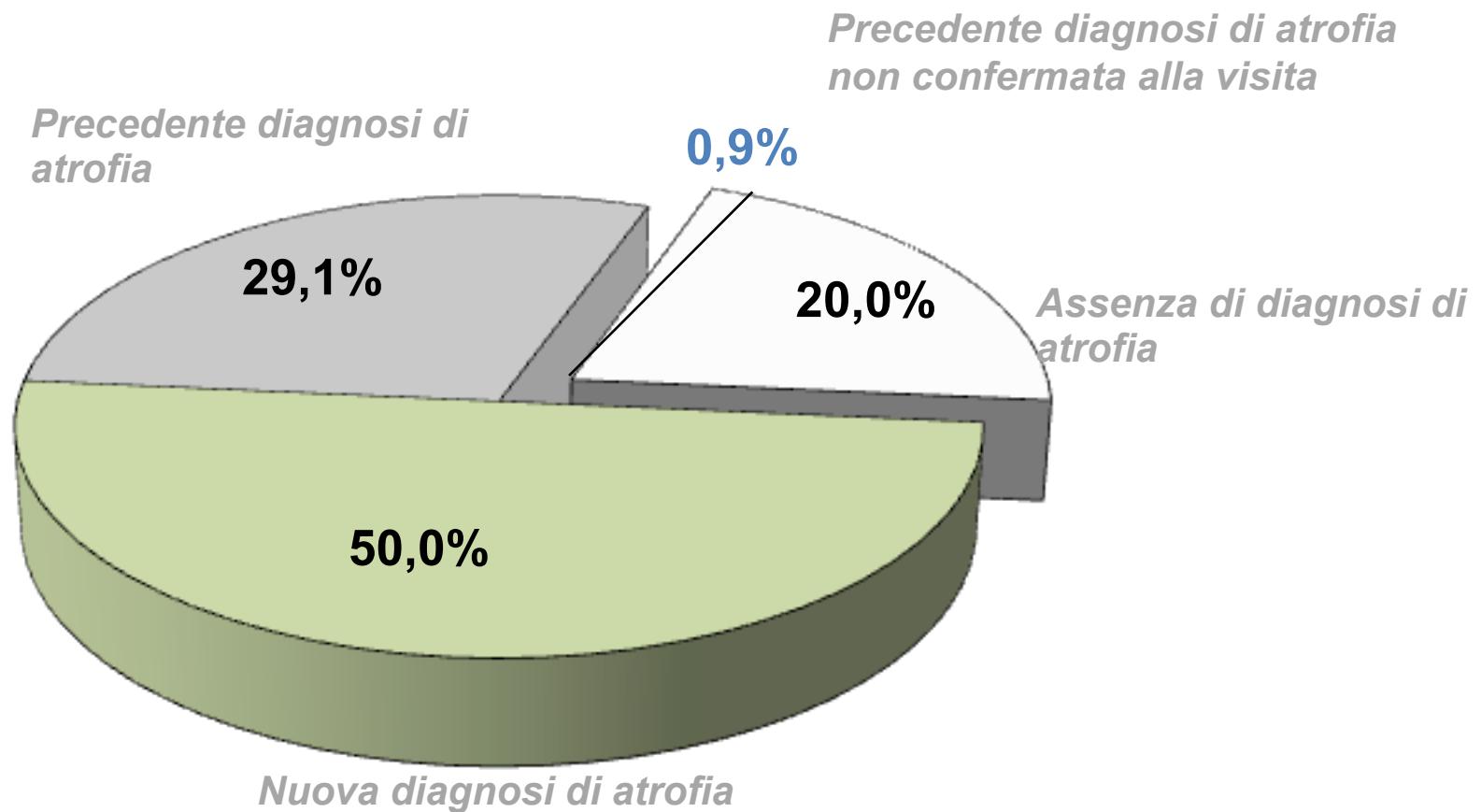
**Atrofia vulvo-vaginale:
epidemiologia e nuove
terapie**

C. Di Carlo

Modificazioni della vagina dopo la menopausa



L'80% delle donne in postmenopausa presenta AVV. I due terzi non aveva ricevuto una diagnosi



Attuale assenza di VVA/GSM 20,9%
Attuale presenza di VVA/GSM 79,1%

Vaginal atrophy of women in postmenopause. Results from a multicentric observational study: The AGATA study

F. Palma ^{a,*}, A. Volpe ^a, P. Villa ^b, A. Cagnacci ^{a,*}, as the writing group of the AGATA study¹

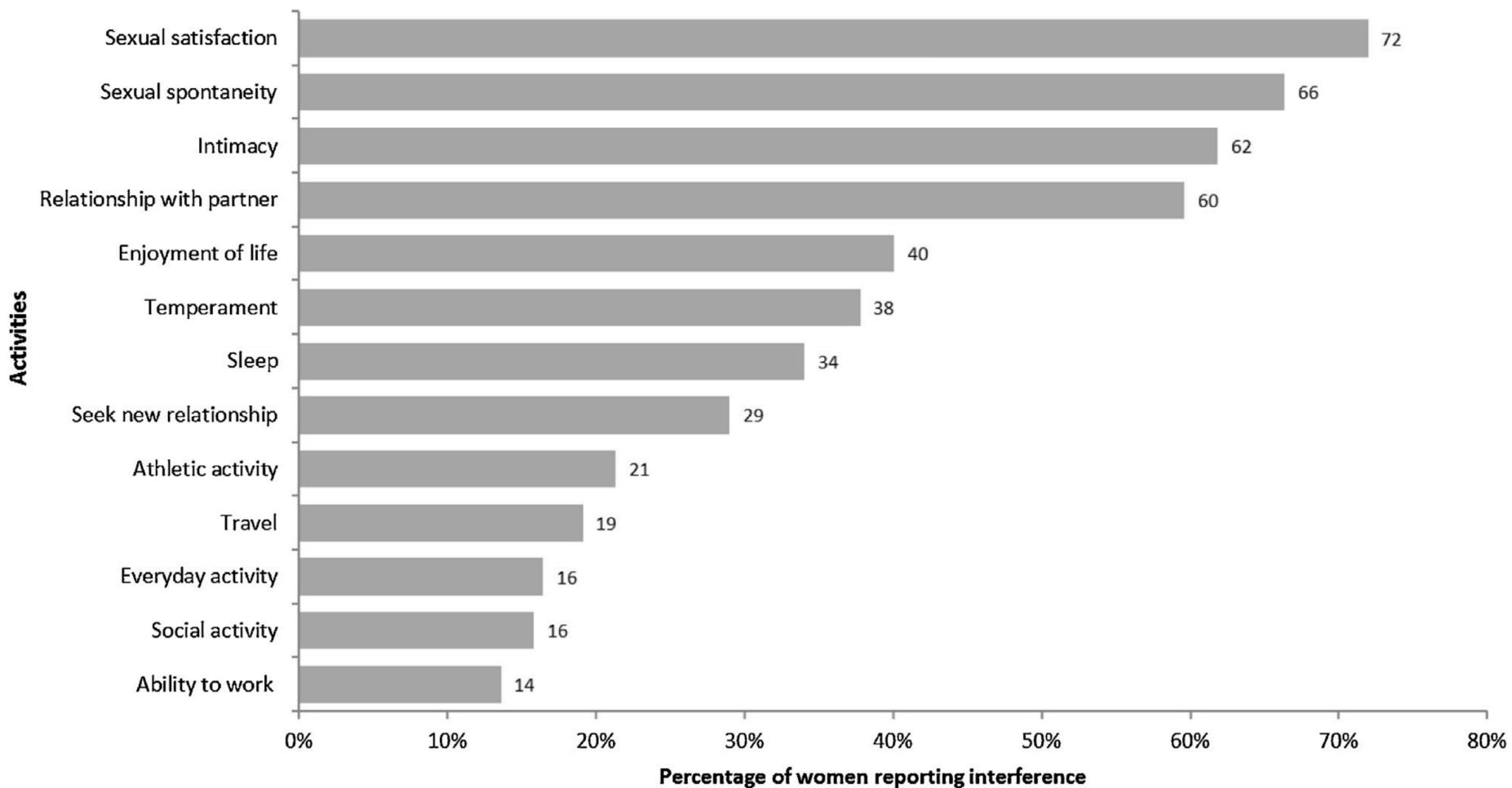
^a Obstetrics and Gynecology, University of Modena and Reggio Emilia, Italy

^b Obstetrics and Gynecology, Policlinico Gemelli of Rome, Italy



Fig. 2. Prevalence of genitourinary menopausal syndrome (GSM) stratified by years since menopause.

Interferenza dell'AVV con la vita sessuale e con altre attività



MENOPAUSA E TERAPIA ORMONALE SOSTITUTIVA

Raccomandazioni della Società Italiana della Menopausa

A cura del Direttivo della Società

Sindrome Genitourinaria della Menopausa

La TOS migliora i sintomi da atrofia urogenitale. La terapia estrogenica vaginale a basso dosaggio è la terapia di scelta per le donne che lamentano unicamente la sindrome genitourinaria. Tutti i preparati estrogenici locali mostrano un'efficacia paragonabile. I preparati estrogenici vaginali per la terapia dell'atrofia urogenitale non richiedono l'associazione progestinica in quanto i dosaggi utilizzati e/o il tipo di estrogeno somministrato (come il promestriene e l'estriolo) non sono in grado di determinare una proliferazione dell'endometrio.

Per il trattamento dei sintomi dell'atrofia vulvovaginale è disponibile ospemifene, un SERM indicato per il trattamento dell'atrofia vaginale, con una efficacia simile a quella delle terapie estrogeniche vaginali.

Terapie ormonali per l'AVV in commercio in Italia

Nome commerciale	Principio attivo	Formulazione	Quantità di principio attivo/die
	Promestriene	Cpr vaginali Crema	10 mg 10 mg
	Estradiolo	Cpr vaginali	0,025 mg
	Estradiolo	Anello vaginale	0,0075 mg
	Estriolo	Ovuli Crema	1 mg 0,5 mg
	Estriolo	Ovuli a rilascio pr.	1 mg
	Estriolo	Crema	0,5 mg
	Estriolo	Gel	0,05 mg
	Estriolo	Ovuli	0,03 mg
	DHEA	Ovuli	6,5 mg
	Ospemifene	Cpr orali	60 mg

Absence of systemic hormonal effects in an oestradiol diether topically active on the vaginal mucosa

J.-P. Wolff ¹, R. Cachelou ¹ and N. Guérinée ^{2,*}

TABLE I

MEAN PLASMA LEVELS OF E₁, E₂, LH AND FSH IMMEDIATELY BEFORE AND AFTER TREATMENT AND SEVERAL DAYS AFTER TREATMENT.

		Before treatment		End of treatment	2-5 Days after treatment
		1st assay	2nd assay		
E1 (pg/ml)	Placebo	53.9 ± 5.8 ^a NS	48.3 ± 5.1 NS NS	51.1 ± 7.7 NS	68.3 ± 15.4
	Colpotrophin	55.1 ± 7.1 NS	55.1 ± 9.8 NS	58.1 ± 9.6 NS	64.4 ± 7.1
	Placebo	18.2 ± 3.3 NS NS	17.2 ± 3.5 NS NS	17.5 ± 3.7 NS	24.5 ± 5.2
	Colpotrophin	25.5 ± 5.7 NS	25.1 ± 5.6 NS	25.7 ± 5.6 NS	24.0 ± 4.1
E2 (pg/ml)	Placebo	30.3 ± 2.8 NS NS	30.1 ± 2.4 NS NS	28.2 ± 2.3 NS	27.4 ± 1.9
	Colpotrophin	27.3 ± 2.1 NS	25.8 ± 3.2 NS	27.1 ± 3.1 NS	26.2 ± 3.4
	Placebo	26.0 ± 1.5 NS NS	27.2 ± 1.5 NS NS	25.7 ± 1.6 NS	25.7 ± 1.6
	Colpotrophin	24.8 ± 1.7 NS	23.8 ± 1.7 NS	22.7 ± 1.6 NS	22.7 ± 1.6

* 0.05 > P > 0.01

NS = P > 0.05.

Effect of one-month treatment with vaginal promestriene on serum estrone sulfate levels in cancer patients: A pilot study

L. Del Pup^{a,*}, D. Postruznik^b, G. Corona^c

Maturitas 72 (2012) 93–94

Patients age, disease and plasma concentrations of E1S before and after promestriene treatment.

Patient	Age	Disease	Pre-E1S (pg/mL)	Post-E1S (pg/mL)
1	63	Cervix	625	616
2	60	Endometrium	217	345
3	63	Vulva	389	447
4	56	Vulva	110	512
5	66	Ovary	853	835
6	59	Endometrium	175	285
7	60	Cervix	130	144
8	45	Ovary	198	232
9	33	Endometrium	502	464
10	48	Cervix	2920	108
11	47	Cervix	57.2	81.5
12	43	Cervix	508	454
13	28	Ovary	22.7	100
14	46	Cervix	1220	856
15	62	Endometrium	69.2	140



THE COCHRANE
COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library.
2006, Issue 4
<http://www.cochranelibrary.wiley.com>

WILEY

Local oestrogen for vaginal atrophy in postmenopausal women (Review)
Copyright © 2006 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Main results

Nineteen trials with 4162 women were included in this review. The overall quality of the studies was good, although not all trials measured the same outcomes. All trials measured efficacy ,with various outcome measures. When comparing the efficacy of different oestrogenic preparations (in the form of creams, pessaries, tablets and the oestradiol-releasing vaginal ring) in relieving the symptoms of vaginal atrophy, results indicated significant findings favouring the cream, ring, and tablets when compared to placebo and non-hormonal gel.

Fourteen trials compared safety. Four looked at hyperplasia, four looked at endometrial overstimulation and seven looked at adverse effects. One trial showed significant adverse effects of the cream (conjugated equine oestrogen) when compared to tablets (oestradiol) which included uterine bleeding, breast pain and perineal pain (1 RCT; OR 0.18, 95% CI 0.07 to 0.50). Two trials showed significant endometrial overstimulation as evaluated by a progestagen challenge test with the cream (conjugated equine oestrogen) group when compared to the ring (OR 0.29, 95% CI 0.11 to 0.78). Although not statistically significant there was a 2% incidence of simple hyperplasia in the ring group when compared to the cream (conjugated equine oestrogen) and 4% incidence of hyperplasia (one simple, one complex) in the cream group (conjugated equine oestrogen) when compared to the tablet (oestradiol).

Eleven studies compared acceptability to the participants by comparing: comfort of product use, ease of use, overall product rating, delivery system and satisfaction. Results showed a significant preference for the oestradiol-releasing vaginal ring.

The therapeutic effect of a new ultra low concentration estriol gel formulation (0.005% estriol vaginal gel) on symptoms and signs of postmenopausal vaginal atrophy: results from a pivotal phase III study

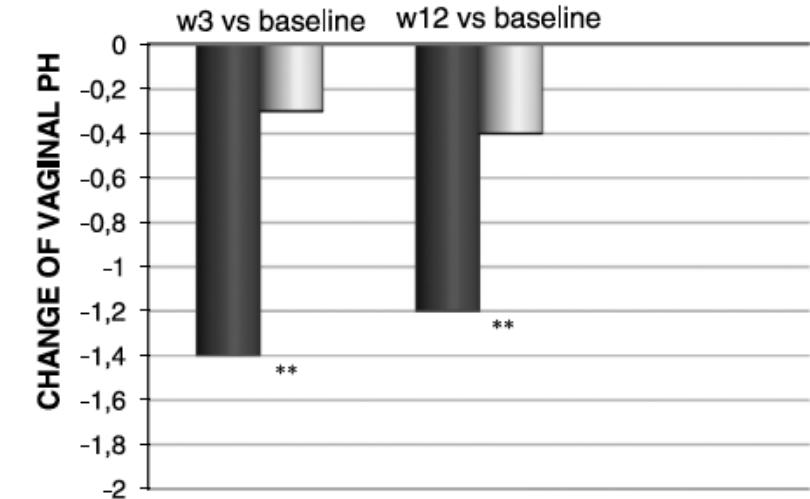
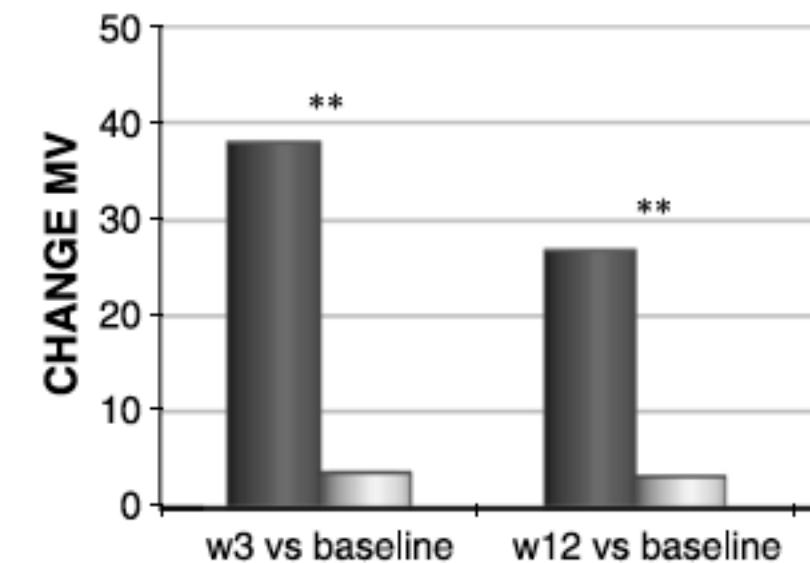
Antonio Cano, MD, PhD,¹ José Estévez, MD,² Ramón Usandizaga, MD, PhD,³ José L. Gallo, MD,⁴ Misericord Guinot, MD, PhD,⁵ Juan L. Delgado, MD,⁶ Elena Castellanos, MD, PhD,⁷ Eloy Moral, MD,⁸ Concepción Nieto, MD, PhD,⁹ Jaime Moscoso del Prado, PhD,¹⁰ and Javier Ferrer, MD, PhD¹¹

R.C.T. di confronto fra 114 pazienti in postmenopausa con atrofia vaginale trattate con gel contenente estriolo (0,05 mg) e 53 trattate con placebo

TABLE 5. Possibly related AEs

	0.005% Estriol gel	Placebo gel
Breast pain	0 (0.0)	1 (1.9)
Vaginal discharge	0 (0.0)	1 (1.9)
Vulvovaginal discomfort	0 (0.0)	1 (1.9)
Application site irritation	1 (0.9)	0 (0.0)
Genital rash	1 (0.9)	0 (0.0)
Vulvovaginal pruritus	5 (4.4)	0 (0.0)
Pruritus	3 (2.6)	2 (3.7)
Candidiasis	1 (0.9)	0 (0.0)
Hyperhydrosis	0 (0.0)	1 (1.9)
Swelling	0 (0.0)	1 (1.9)
Hot flush	0 (0.0)	3 (5.7)
Abdominal pain	1 (0.9)	1 (1.9)
Sensation of leg heaviness	0 (0.0)	1 (1.9)

Data are presented as n (%) of women with the AE.
AE, adverse event.



* p NS, Wilcoxon Rank sum test

** p<0.001, Wilcoxon Rank sum test

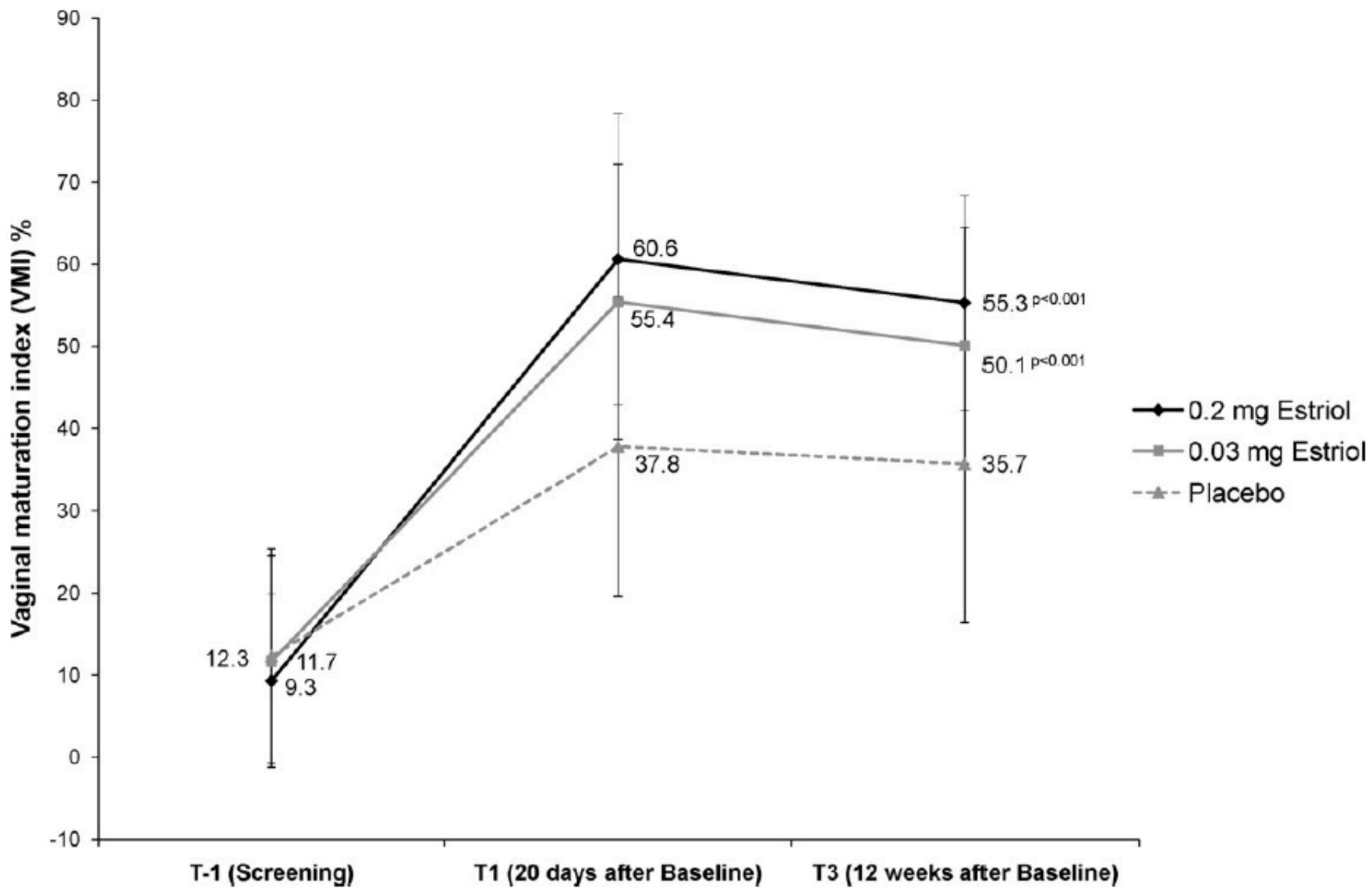


Fig. 2. Improvement in vaginal maturation index. P-values (Wilcoxon–Mann–Whitney U test) are given for the comparison of verum and placebo.

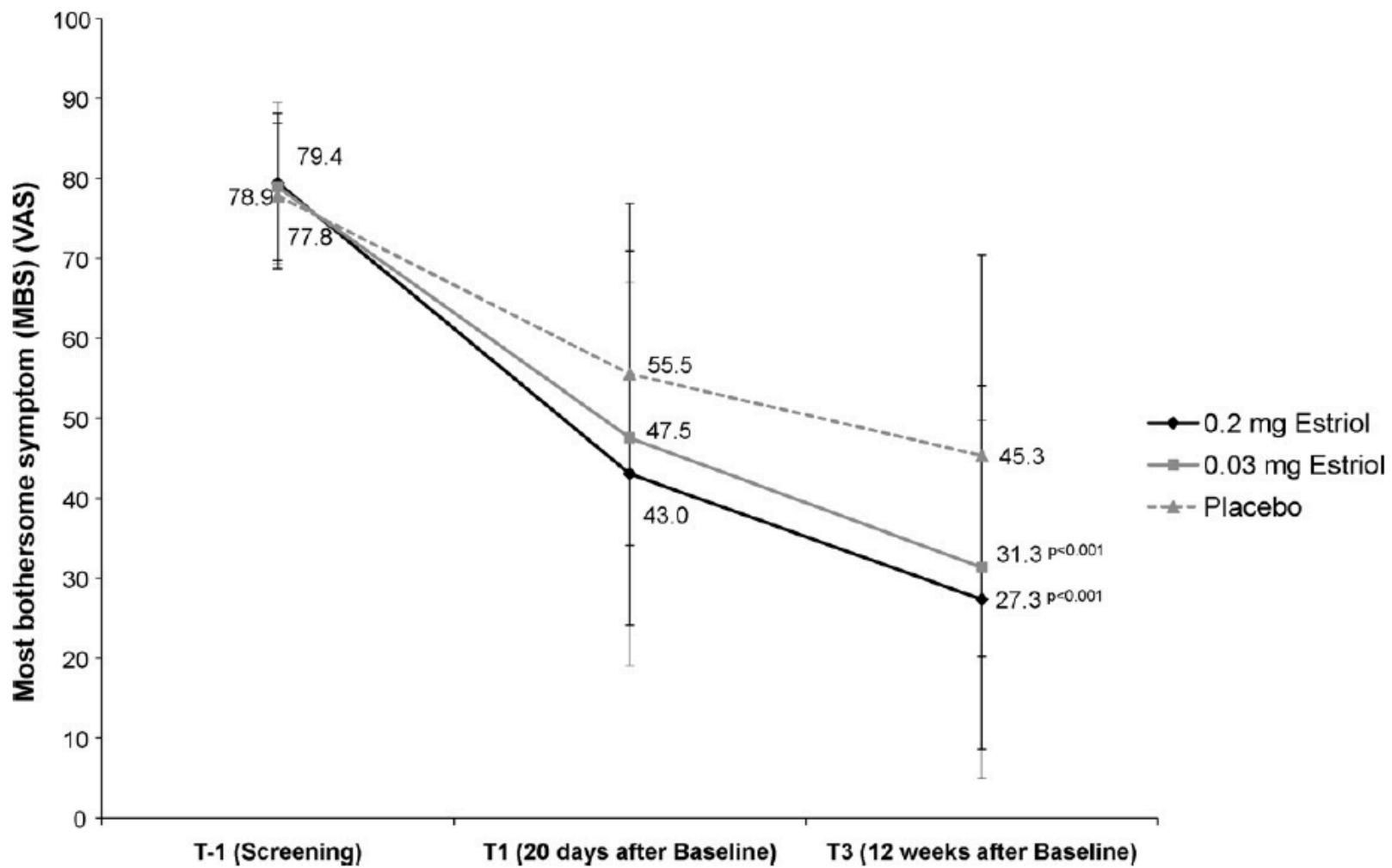


Fig. 4. Improvement in severity of most bothersome symptom. *P*-values (Wilcoxon–Mann–Whitney U test) are given for the comparison of verum and placebo.

SERMs nella pratica clinica

CLOMIFENE

- Terapia dell'anonovulazione

TAMOXIFENE

- Terapia endocrina del carcinoma mammario

RALOXIFENE

- Terapia e prevenzione dell'osteoporosi

BAZEDOXIFENE

Terapia dell'AVV

OSPEMIFENE

Ospemifene ha effetti sia agonisti che antagonisti

Cervello

- Effetto **agonista**/estrogenico in studi pre-clinici

Epitelio vaginale

- Effetto **agonista**/estrogenico

Osso

- Effetto **agonista**/estrogenico in studi pre-clinici

Endometrio uterino

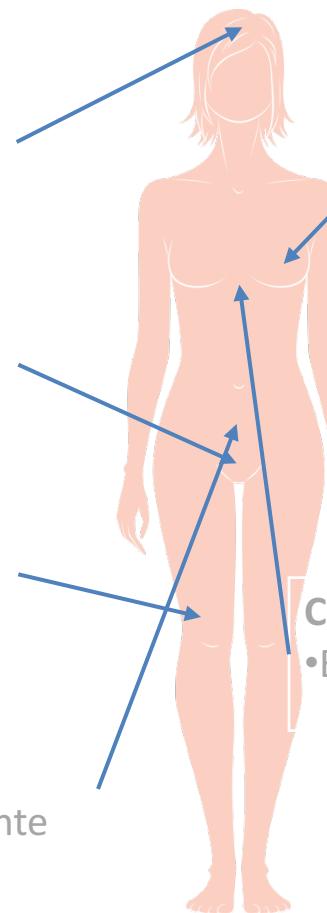
- Azione complessivamente **neutra**¹

Mammella

- Effetto **antagonista**/antiestrogenico in studi pre-clinici

Cuore

- Effetto complessivamente **neutro**



Ospemifene 12-month safety and efficacy in postmenopausal women with vulvar and vaginal atrophy

S. R. Goldstein*, G. A. Bachmann†, P. R. Koninckx‡, V. H. Lin***, D. J. Portman††, O. Ylikorkala††
and the Ospemifene Study Group

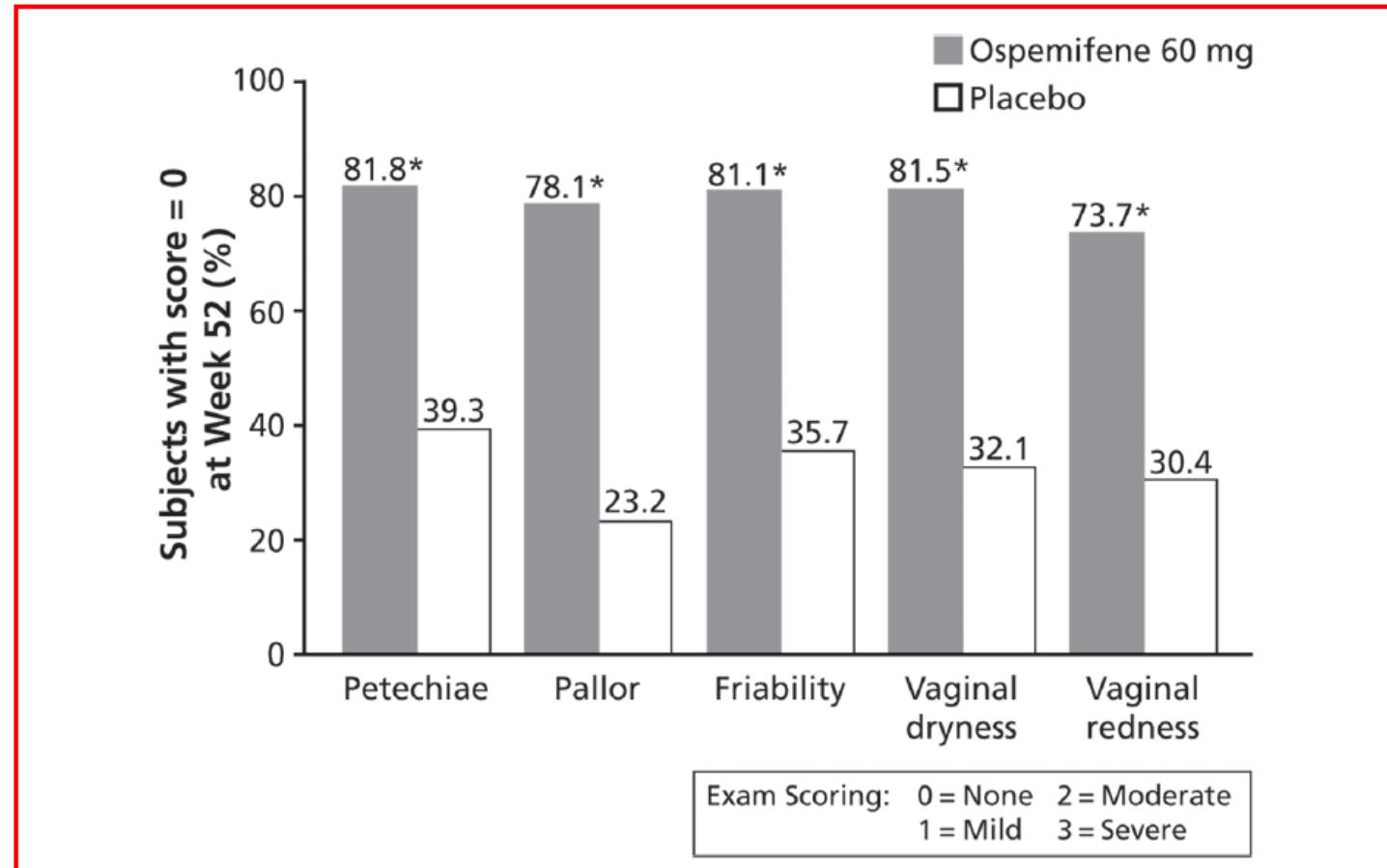


Figure 3 Visual evaluation of the vagina; percentage of subjects with no abnormalities at week 52 (observed cases; intent-to-treat population).
*, $p < 0.0001$

Ospemifene 12-month safety and efficacy in postmenopausal women with vulvar and vaginal atrophy

S. R. Goldstein*, G. A. Bachmann†, P. R. Koninckx‡, V. H. Lin***, D. J. Portman††, O. Ylikorkala††
and the Ospemifene Study Group

Table 3 Endometrium histological biopsy characteristics: baseline vs. week 52 (last observation carried forward)*. Data are given as *n* (%)

<i>Histological characteristics</i> [†]	<i>Ospemifene 60 mg/day</i>		<i>Placebo (n = 62)</i>	
	<i>Baseline</i>	<i>Week 52[‡]</i>	<i>Baseline</i>	<i>Week 52</i>
Tissue insufficient for diagnosis	59 (16.2)	27 (8.7)	8 (12.9)	11 (19.6)
Atrophic	300 (82.4)	267 (86.1)	52 (83.9)	45 (80.4)
Inactive	1 (0.3)	1 (0.3)	1 (1.6)	0 (0)
Weakly proliferative	1 (0.3)	7 (2.3)	0 (0)	0 (0)
Active proliferative	0 (0)	3 (1.0)	0 (0)	0 (0)
Hyperplasia	0 (0)	1 (0.3)	0 (0)	0 (0)

Ospemifene 12-month safety and efficacy in postmenopausal women with vulvar and vaginal atrophy

S. R. Goldstein*, G. A. Bachmann†, P. R. Koninckx‡, V. H. Lin***, D. J. Portman††, O. Ylikorkala††
and the Ospemifene Study Group

Table 2 Summary of treatment-emergent adverse events (TEAEs) occurring in $\geq 5\%$ of subjects in the ospemifene 60 mg/day group. Data are given as n (%). Note: Counts include adverse events that were ongoing from the 12-week pivotal safety study

	<i>Ospemifene</i> 60 mg/day ($n = 364$) [*]	<i>Placebo</i> ($n = 62$) [*]
TEAE	308 (84.6)	47 (75.8)
Withdrawals due to adverse events	49 (13.5)	6 (9.7)
Serious TEAEs	18 (4.9)	4 (6.5)
<i>Most frequent TEAEs</i>		
Urinary tract infection	61 (16.8)	15 (24.2)
Hot flush	46 (12.6)	4 (6.5)
Nasopharyngitis	36 (9.9)	4 (6.5)
<i>Other TEAEs</i>		
Vaginal candidiasis and/or vulvovaginal mycotic infection	35 (9.6)	2 (3.2)
Headache	33 (9.1)	6 (9.7)
Muscle spasms	31 (8.5)	4 (6.5)
Back pain	24 (6.6)	2 (3.2)
Hyperhidrosis	22 (6.0)	5 (8.1)
Vaginal discharge	20 (5.5)	0 (0)
Insomnia	19 (5.2)	0 (0)
Cystitis	19 (5.2)	0 (0)

La storia dell'introcrinologia

Inizia con la scoperta che le cellule della prostata normale e dei tumori prostatici sono in grado di sintetizzare androgeni **al loro interno**

Labrie et al., Clin. Invest. Med. 5, 267-275, 1982;
Labrie et al., Important Adv Oncol, 193-217, 1985.
Labrie Mol. Cell. Endocrinol 1, C113-C118, 1991.



Not logged in [Talk](#) [Contributions](#) [Create account](#) [Log in](#)

Read [Edit](#) [View history](#)

Fernand Labrie

From Wikipedia, the free encyclopedia

Fernand Labrie, OC OQ MSRC (June 28, 1937 – January 16, 2019) was a Canadian medical researcher who specializes in endocrinological research and prostate cancer research.

Early life [edit]

Born in Laurierville, Quebec, he received a Bachelor of Arts degree in 1957 from the Séminaire de Québec. He received his Doctor of Medicine in 1962 and a Ph.D. in 1966 from Université Laval. From 1966 to 1969, he took his postdoctoral studies at the University of Cambridge and the University of Sussex.^[1]

In 1966, he joined the faculty of Université Laval as an Assistant Professor. In 1969 he was made an Associate Professor, and in 1974 he was made a Full Professor. In 1990, he was made the Head of the Department of Physiology. In 1969, he was made the Director of the Molecular Endocrinology Research Centre.^[1] Labrie died at the age of 81 in January 2019.^[2]

Honours [edit]

In 1981, he was made an Officer of the Order of Canada in recognition for being "one of the leading authorities in contemporary endocrinological research".^[3] In 1991, he was made an Officer of the National Order of Quebec. In 1990, he was awarded the Government of Quebec's Prix Michel-Sarrazin. In 1998, he was awarded the Izaak-Walton-Killam Award. In 2007, he was awarded the King Faisal International Prize.

References [edit]

1. ^ ^a ^b Elizabeth Lumley, ed. (July 1997). *Canadian Who's Who 1997: Volume 32*. University of Toronto Press. ISBN 0802049966.
2. ^ "Le Dr Fernand Labrie s'est éteint à 81 ans" (in French). radio-canada.ca. 17 January 2019. Retrieved 17 January 2019.
3. ^ "Order of Canada citation" (in).

Authority control BIBSYS: 90375399 · BNF: cb119104156 (data) · CINII: DA02569022 · ISNI: 0000 0000 8078 6541 · LCCN: n84140373 · NKC: ola2004235478 · ORCID: 0000-0003-4825-8767 · SUDOC: 026957698 · VIAF: 13135 · WorldCat Identities (via VIAF): 13135

Categories: 1937 births | 2019 deaths | Canadian medical researchers | Canadian endocrinologists | Fellows of the Royal Society of Canada | Officers of the National Order of Quebec | Officers of the Order of Canada | Université Laval faculty | Université Laval alumni | People from Centre-du-Québec

This page was last edited on 26 February 2019, at 01:02 (UTC).
Text is available under the [Creative Commons Attribution-ShareAlike License](#); additional terms may apply. By using this site, you agree to the [Terms of Use](#) and [Privacy Policy](#). Wikipedia® is a registered trademark of the [Wikimedia Foundation, Inc.](#), a non-profit organization.

[Privacy policy](#) [About Wikipedia](#) [Disclaimers](#) [Contact Wikipedia](#) [Developers](#) [Cookie statement](#) [Mobile view](#)

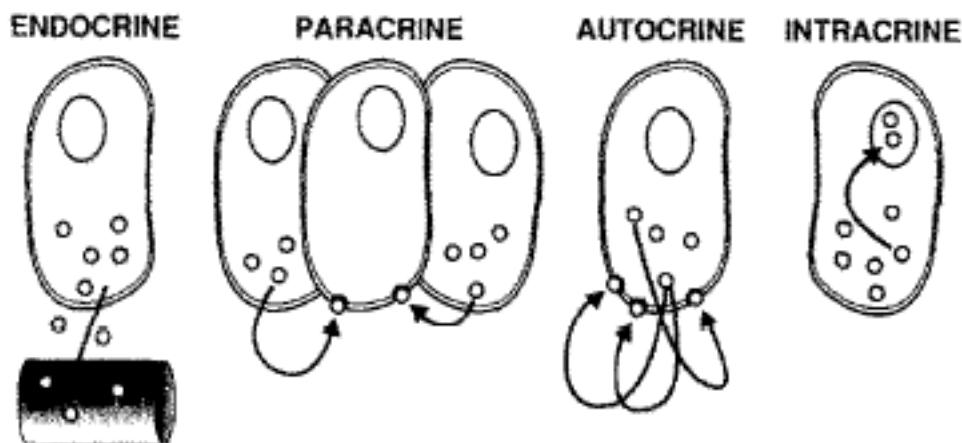
 

MOLCEL 02559

At the Cutting Edge

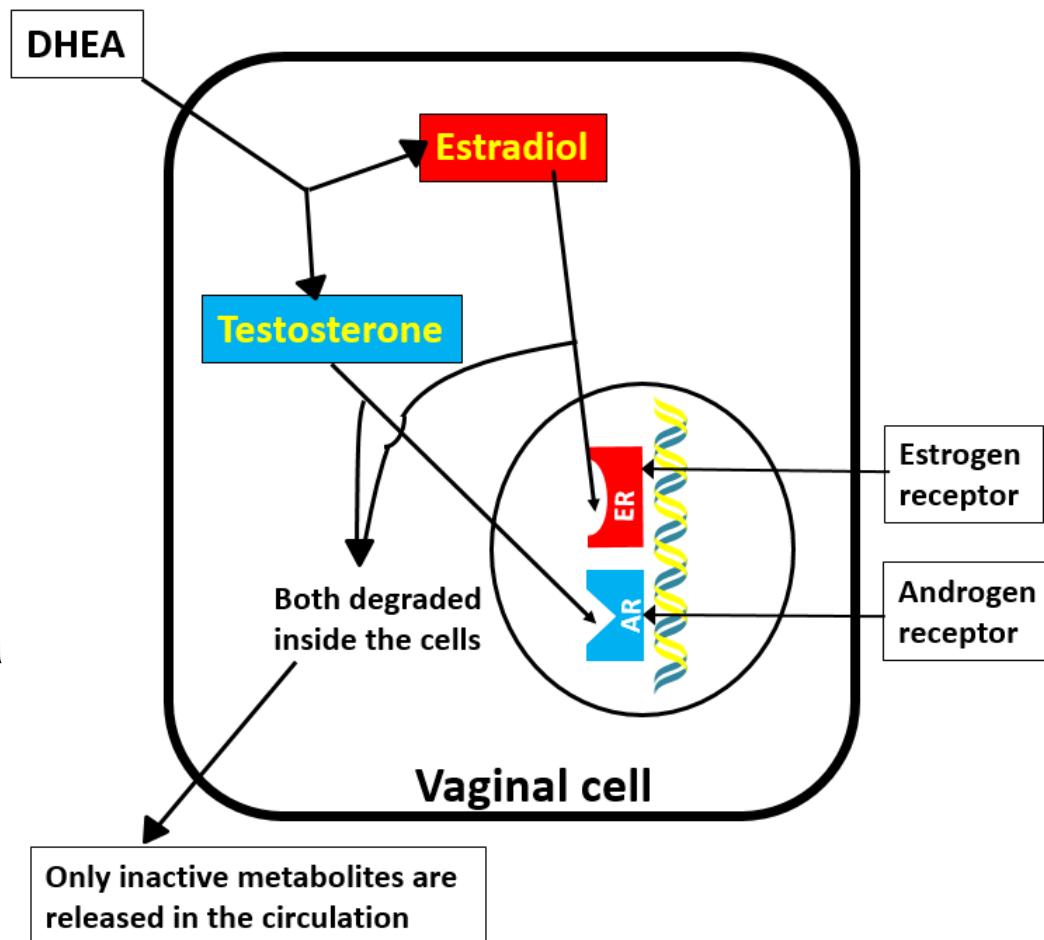
Introcrinology

Fernand Labrie



Introcrinologia

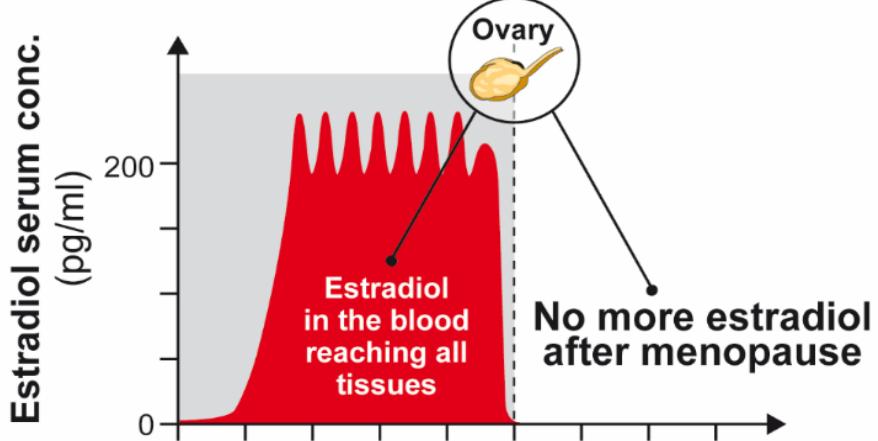
Sintesi intracellulare di estradiolo e testosterone a partire dal DHEA seguita dalla loro azione e dalla loro inattivazione a livello locale, con successiva escrezione di metaboliti inattivi. Si evita così qualsiasi azione a livello di altre cellule in altri tessuti.



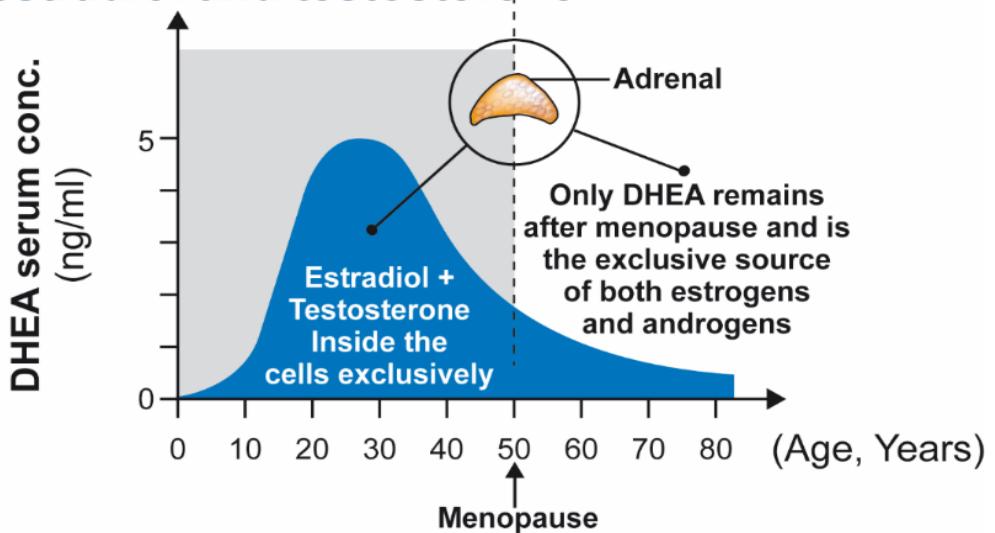
Since ovarian estrogen secretion stops in all women at menopause, and not all women suffer from the menopausal symptoms and signs mentioned above, there must be another factor or another variable source of sex steroids which could explain why some women are clinically free from menopausal symptoms while others (about 75%) suffer from menopausal symptoms and signs at various degrees [10–12].

Prima della menopausa gli steroidi sessuali originano da due fonti

A- Estradiol (from the ovary) which is secreted in the blood to reach all tissues

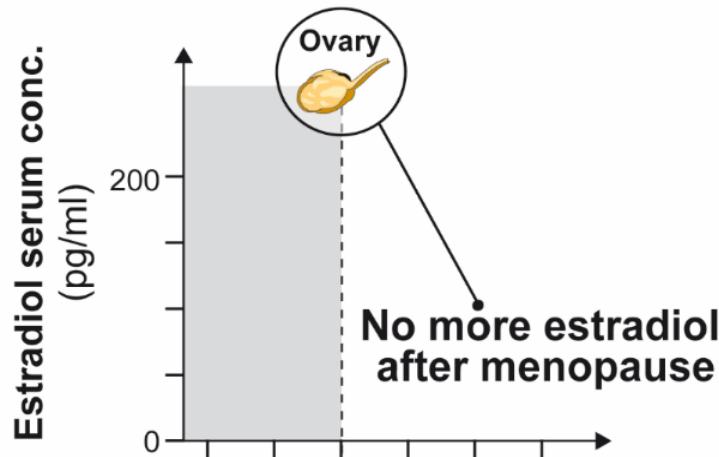


B- DHEA (mainly from the adrenals) for the tissue-specific intracellular formation of estradiol and testosterone

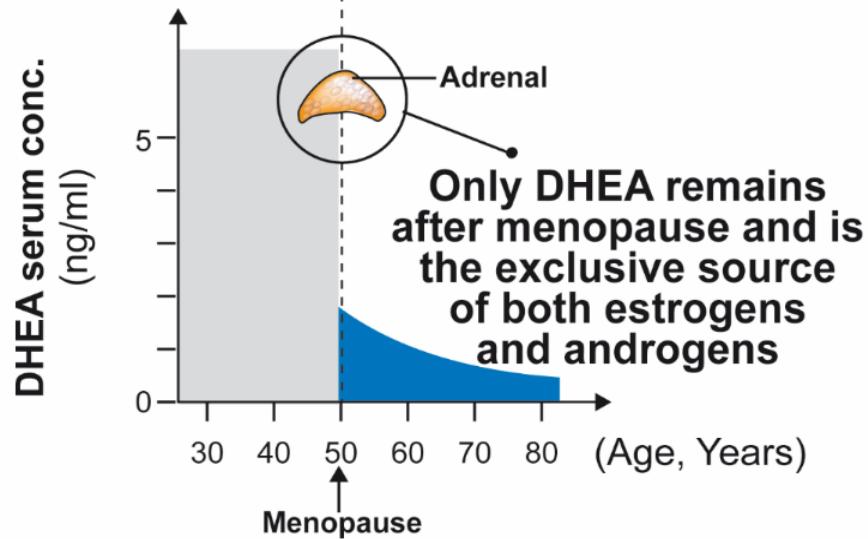


Dopo la menopausa il DHEA (principalmente di origine surrenalica è l'unica fonte di steroidi sessuali

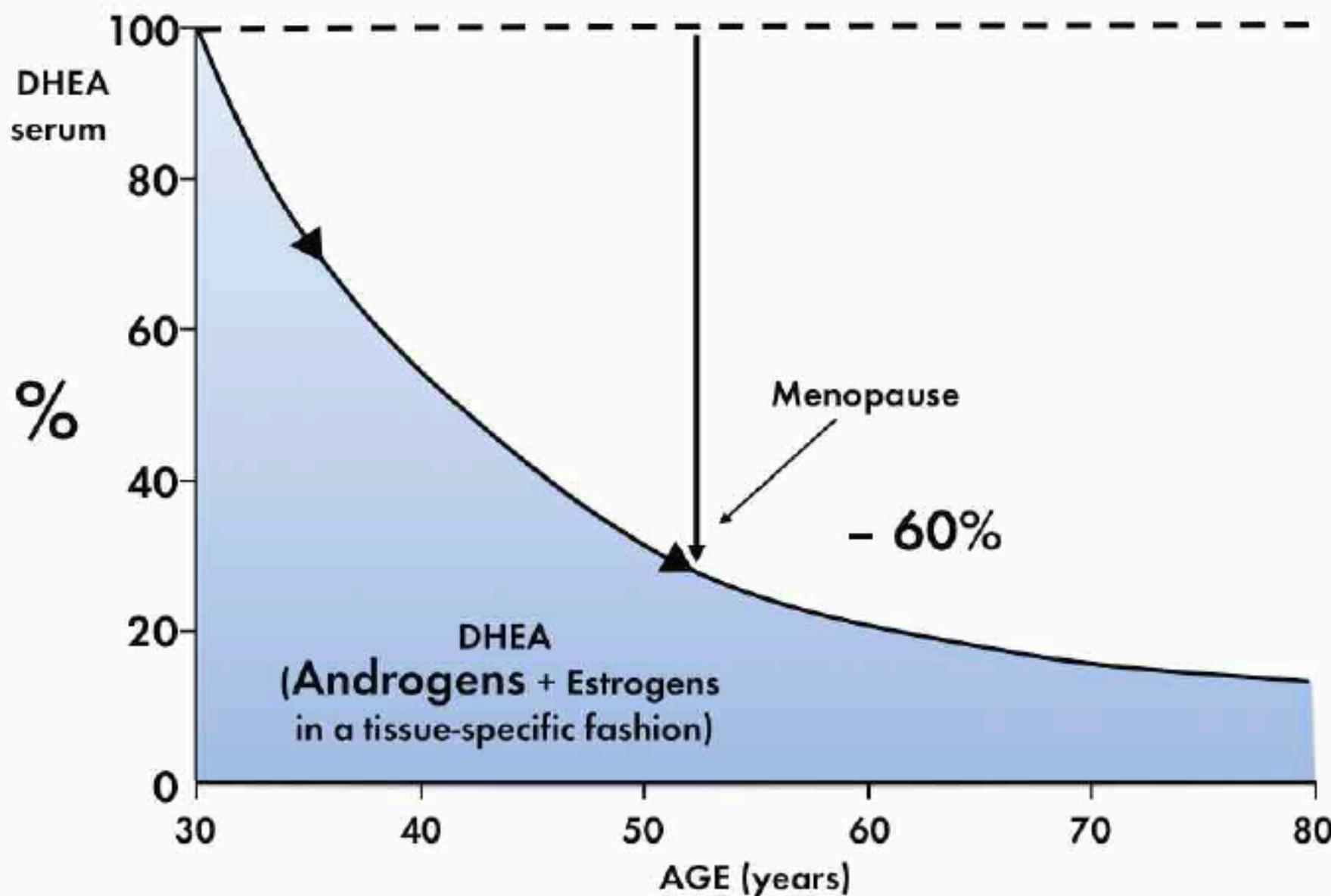
A- Estradiol (from the ovary)



B- DHEA (mainly from the adrenals) for the tissue-specific intracellular formation of estradiol and testosterone



Rationale for DHEA



L'efficacia e la sicurezza del DHEA per via vaginale sono stati valutati in una serie di studi clinici. Studi fondamentali

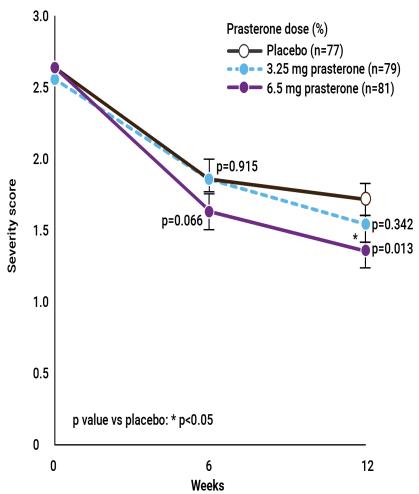
Study ID	Type of study/design	Dose(s) evaluated	Objective	Duration	Study population	Primary endpoint	Mean age (age range), gender, ethnicity, mean BMI or weight
ERC-231 (PIVOTAL)	Phase III study Randomized, double-blind, placebo- controlled Multi centre	Placebo Prasterone: •3.25mg (0.25%) – off licence •6.5mg (0.50%) Once daily	To confirm the efficacy of intravaginal prasterone on the symptoms and signs of vaginal atrophy	12 weeks	255 subjects enrolled Postmenopausal women with vaginal atrophy; dyspareunia as MBS	4 co-primary endpoints (vaginal maturation index*, vaginal pH, improvement in MBS)	59 years (40–75 years)/ 100% Female/ 92% White/ BMI = 26.1
ERC-238 (PIVOTAL)	Phase III study Randomized, double-blind, placebo- controlled Multi centre	Placebo Prasterone: 6.5mg (0.50%) Once daily	To confirm the efficacy of intravaginal prasterone on moderate to severe pain at sexual activity (dyspareunia) as MBS of vulvovaginal atrophy	12 weeks	558 subjects enrolled Postmenopausal women with vaginal atrophy; dyspareunia as MBS	4 co-primary endpoints (vaginal maturation index*, vaginal pH, improvement in MBS)	59 years (40–80 years)/ 100% Female/ 91% White/ BMI = 26.4
ERC-230 LONG TERM (PIVOTAL)	Phase III Open-label Multi centre	Prasterone: 6.5mg (0.50%) Once daily	To assess the long-term safety of intravaginal prasterone	52 weeks	530 subjects enrolled Post-menopausal women having self-identified at least one mild to severe vaginal atrophy symptom	Endometrial biopsies and serum DHEA and DHEA metabolite levels	58 years (43–75 years)/ 100% Female/ 92% White/ BMI = 26.3

L'efficacia e la sicurezza del DHEA per via vaginale sono stati valutati in una serie di studi clinici. Studi secondari.

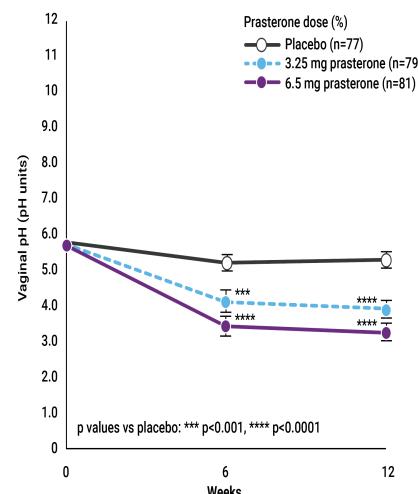
Study ID	Type of study/design	Dose(s) evaluated	Objective	Duration	Study population	Primary endpoint	Mean age (age range), gender, ethnicity, mean BMI or weight
ERC-213	Phase I/II PK study Randomized, double-blind, placebo-controlled Single centre	Placebo •Prasterone: •6.5mg (0.50%) •13.0mg (1.0%) – off licence •13.4mg (1.8%) – off licence Once daily	Systemic bioavailability of DHEA and its metabolites and the PK of vaginal suppositories at four different DHEA concentrations	7 days	40 subjects enrolled Postmenopausal women with vaginal atrophy	PK parameters	62 years (44–72 years)/ 100% Female/ 99% White/ Weight = 64 kg
ERC-210	Phase III study Randomized, double-blind, placebo-controlled Multi centre	Placebo •Prasterone: •3.25mg (0.25%) – off licence •6.5mg (0.50%) •13.0mg (1.0%) – off licence Once daily	To determine the dose-response of vaginal mucosa parameters to the local action of DHEA	12 weeks	218 subjects enrolled Postmenopausal women with vaginal atrophy	4 co-primary endpoints (vaginal maturation index*, vaginal pH, improvement in MBS)	58 years (42–74 years)/ 100% Female/ 100% White/ BMI = 26
ERC-234	Phase III study Randomized, double-blind, placebo-controlled Multi centre	Placebo •Prasterone: •3.25mg (0.25%) – off licence •6.5mg (0.50%) Once daily for 2 weeks followed by twice weekly for 10 weeks – off license	To analyze the efficacy of intravaginal prasterone on vaginal dryness	12 weeks	450 subjects enrolled Postmenopausal women with vaginal atrophy; dryness as MBS	4 co-primary endpoints (vaginal maturation index*, vaginal pH, improvement in MBS)	58 years (41–75 years)/ 100% Female/ 90% White/ BMI = 26.9

ERC-231: donne in post menopausa con AVV e con dispareunia come sintomo più fastidioso

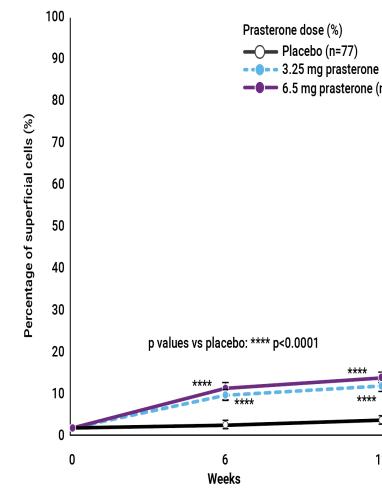
Gravità della dispareunia



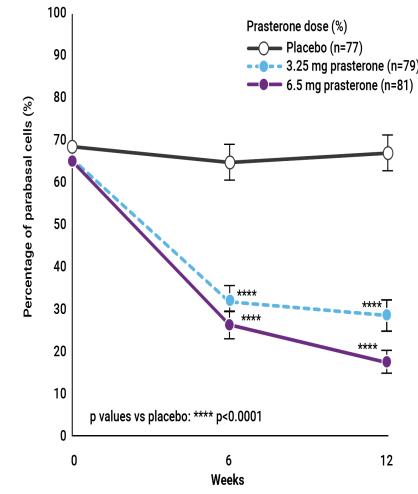
pH vaginale



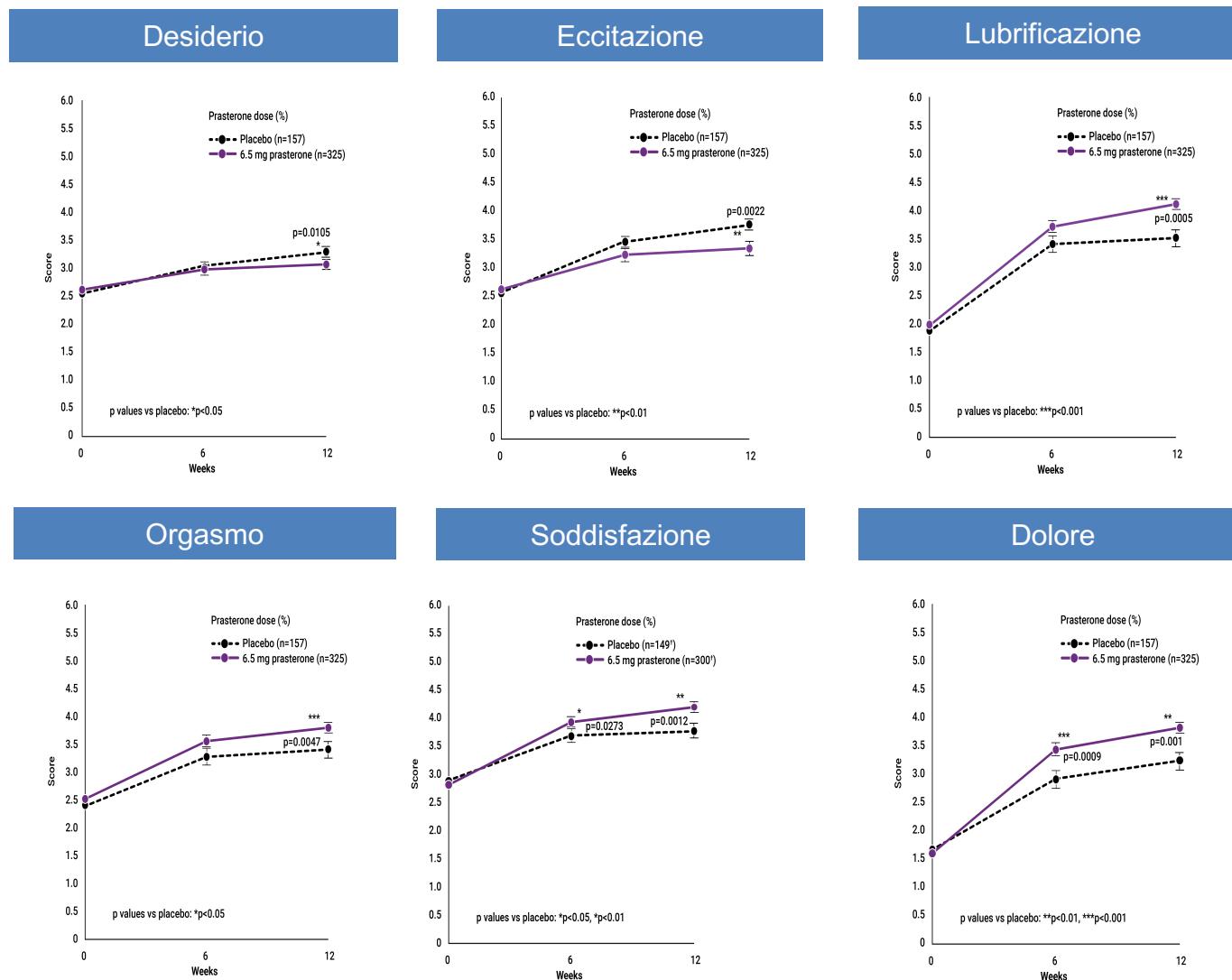
% cellule superficiali



% cellule parabasali



ERC-238: donne in post menopausa con AVV e con dispareunia come sintomo più fastidioso. Effetti sulla funzione sessuale (FSFI)



ERC-230: Studio di sicurezza. 389 donne in post menopausa con AVV lieve, moderata o severa trattate con 6.5 mg di prasterone per 52 settimane

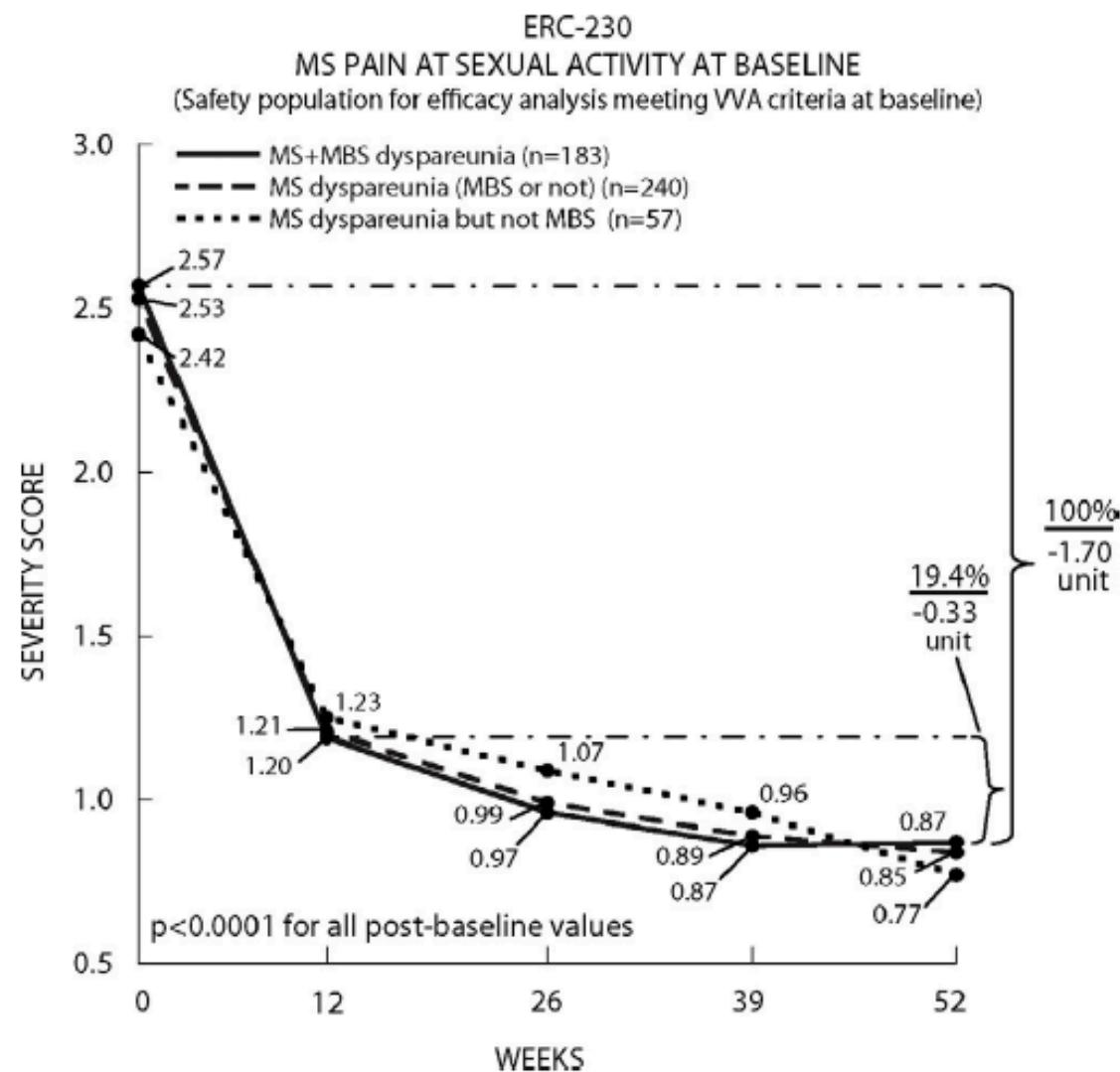
Istologia endometriale

- **385 (99%) endometrio atrofico**
- **4 (1%) endometrio inattivo**

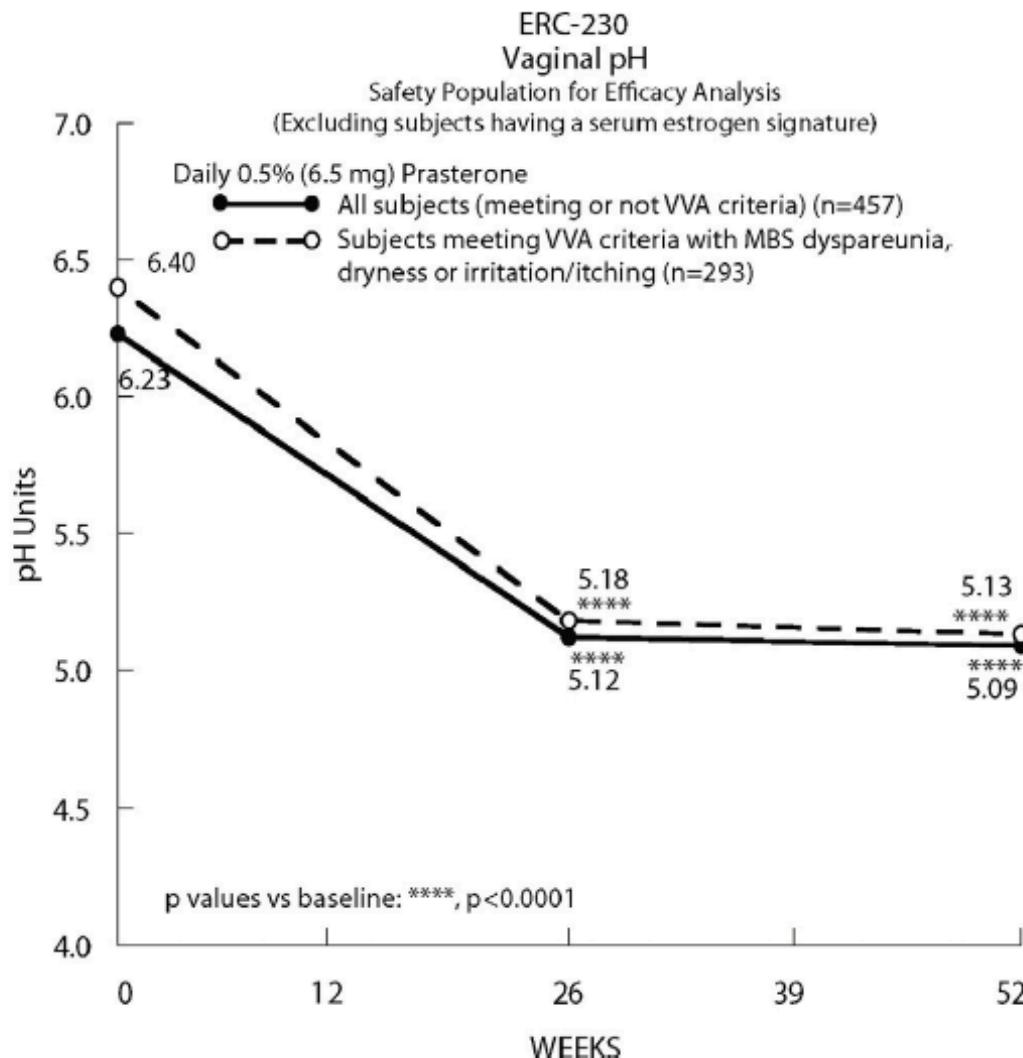
Valutazione ecografica dell'endometrio

- **Nessuna modifica dello spessore endometriale**

ERC-230: Studio di sicurezza. 389 donne in post menopausa con AVV lieve, moderata o severa trattate con 6.5 mg di prasterone per 52 settimane

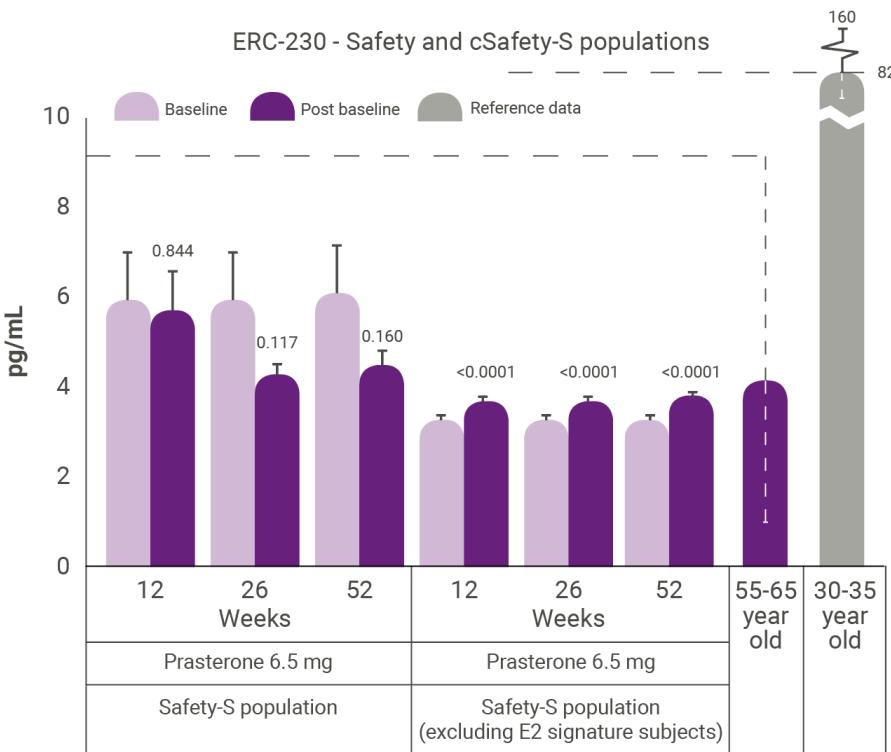


ERC-230: Studio di sicurezza .389 donne in post menopausa con AVV lieve, moderata o severa trattate con 6.5 mg di prasterone per 52 settimane

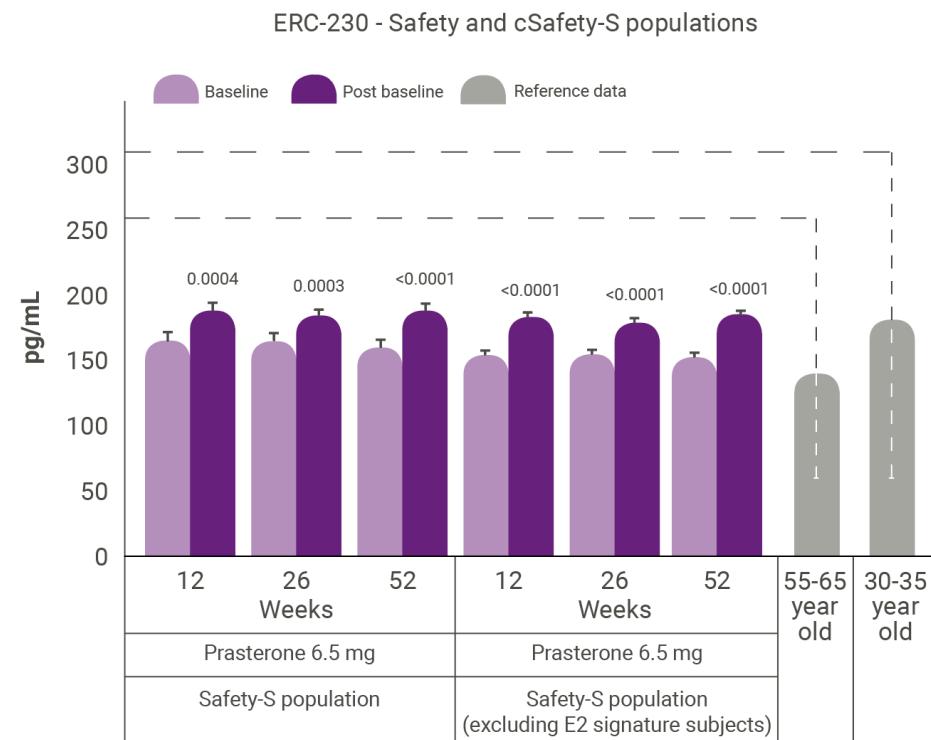


ERC-230: Studio di sicurezza .389 donne in post menopausa con AVV lieve, moderata o severa trattate con 6.5 mg di prasterone per 52 settimane

Serum concentrations of oestradiol in Safety-S and cSafety-S populations



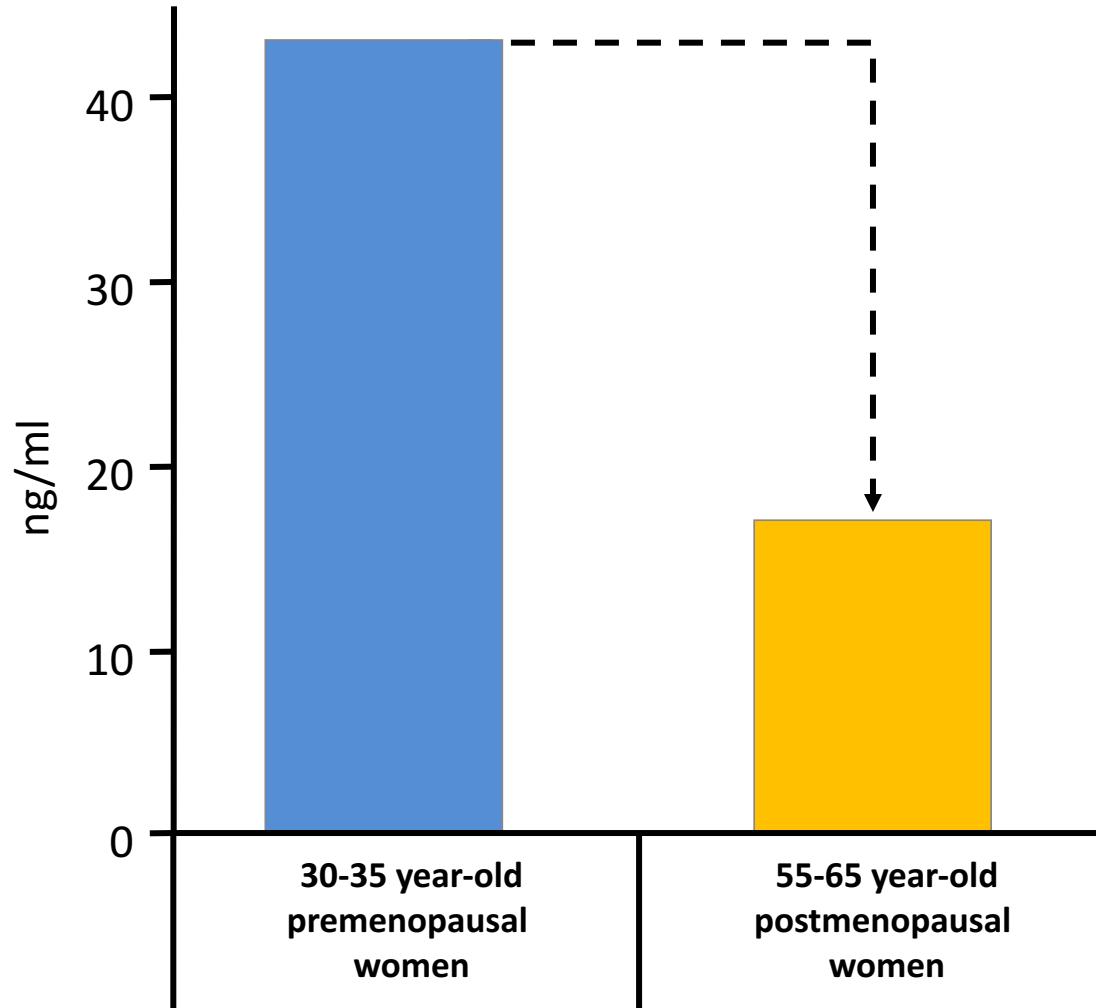
Serum concentrations of testosterone in Safety-S and cSafety-S populations

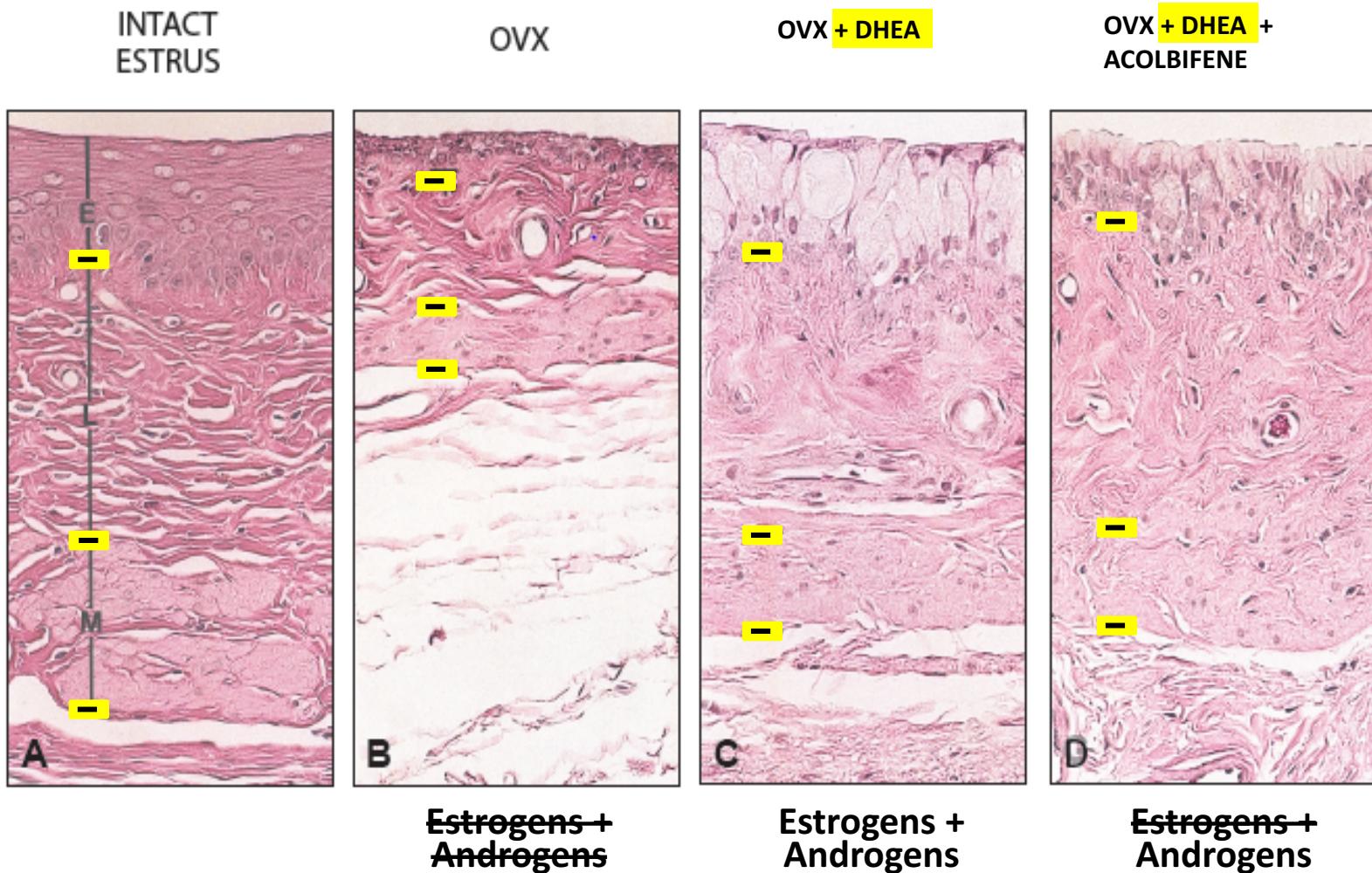


Non ci sono dati su donne con:

- Iperplasia endometriale
- Endometriosi
- Cancro mammario attivo o pregresso
- Cancro ovarico attivo o pregresso
- PAP test anomalo
- TVP attiva o pregressa
- Ipertensione non controllata
- Trombosi arteriosa attiva o pregressa
- In TOS estrogenica, estroprogestinica o androgenica

In postmenopausa gli androgeni totali diminuiscono del 60%





Both androgens and estrogens are responsible for vaginal health

“Consequently, treatment with estrogens is only a partial treatment.

DHEA makes estrogens and androgens in the three layers of the vagina with an exclusive androgenic action in the nerve endings possibly responsible for the benefits of intravaginal DHEA on sexual dysfunction.”

Tutte le slides sono disponibili su

www.costantinodicarlo.it

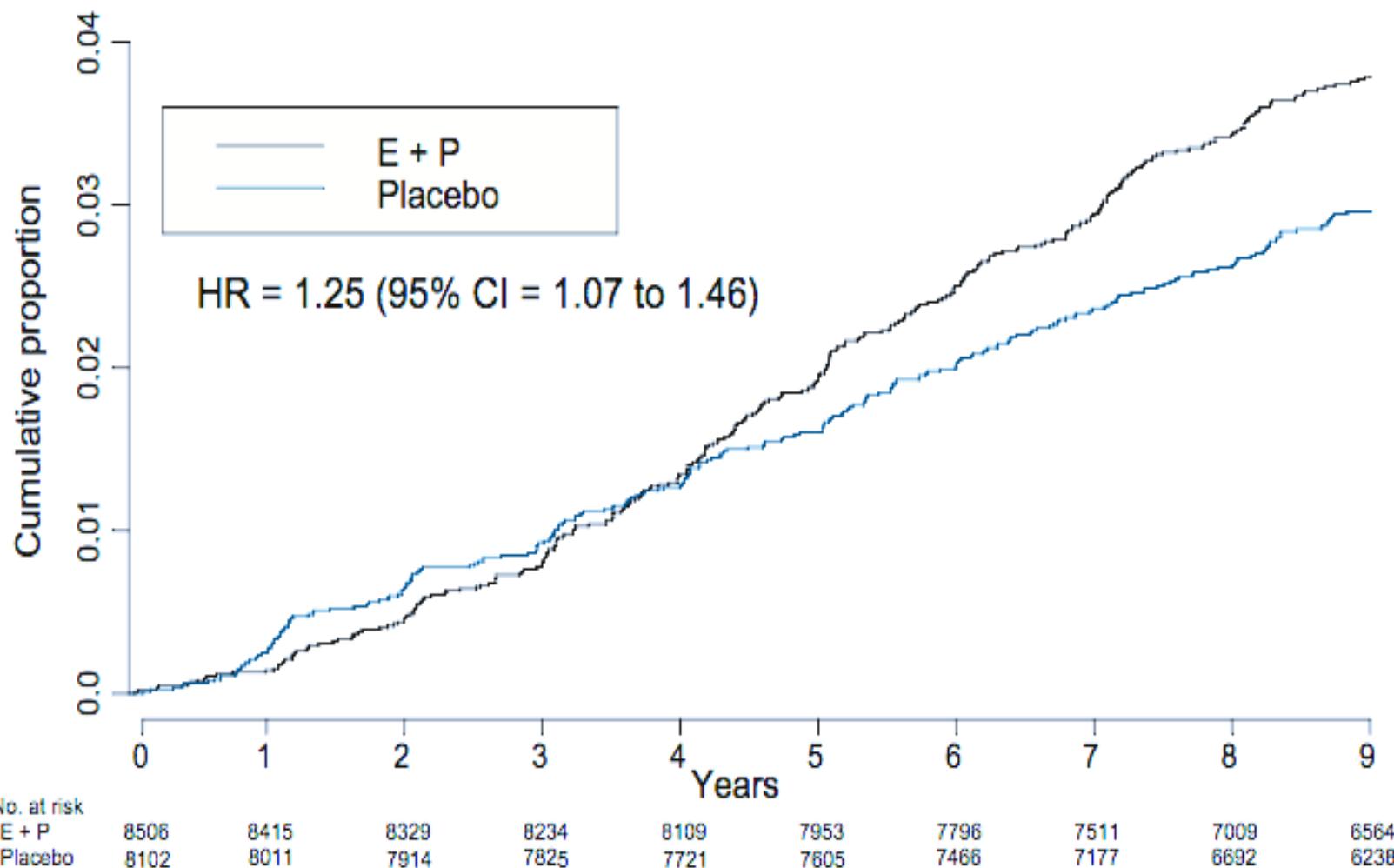
Changing Concepts: Menopausal Hormone Therapy and Breast Cancer

Rowan T. Chlebowski, Garnet L. Anderson

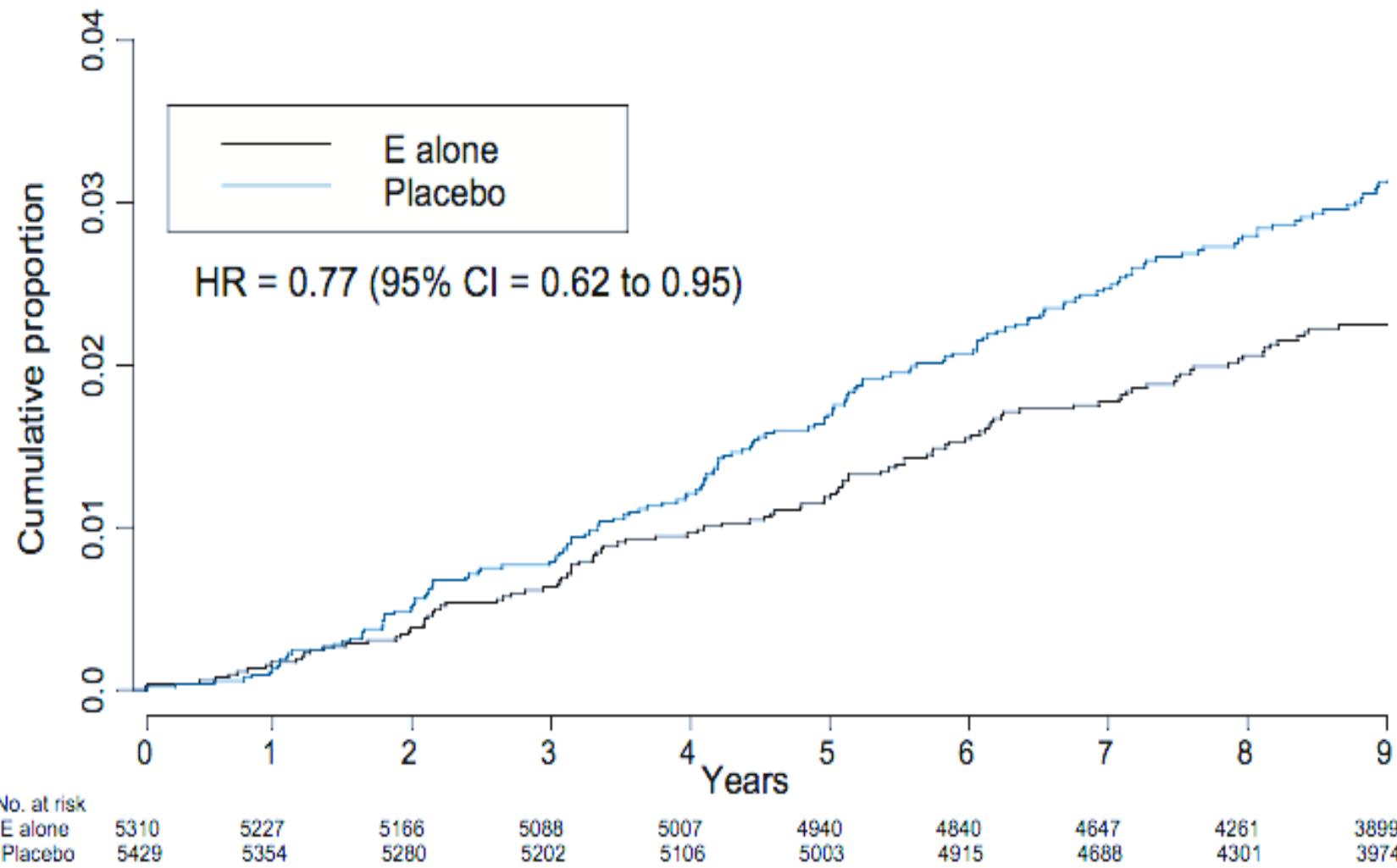
Manuscript received September 16, 2011; revised December 20, 2011; accepted January 2, 2012.

Correspondence to: Rowan T. Chlebowski, MD, PhD, Los Angeles Biomedical Research Institute at Harbor, UCLA Medical Center, 1124 W. Carson St, Torrance, CA 90502 (e-mail: rowanchlebowski@gmail.com).

HR for invasive breast cancer among women receiving CEE+MAP in the WHI study



HR for invasive breast cancer among women receiving only CEE in the WHI study



Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence



*Collaborative Group on Hormonal Factors in Breast Cancer**



www.thelancet.com Published online August 29, 2019

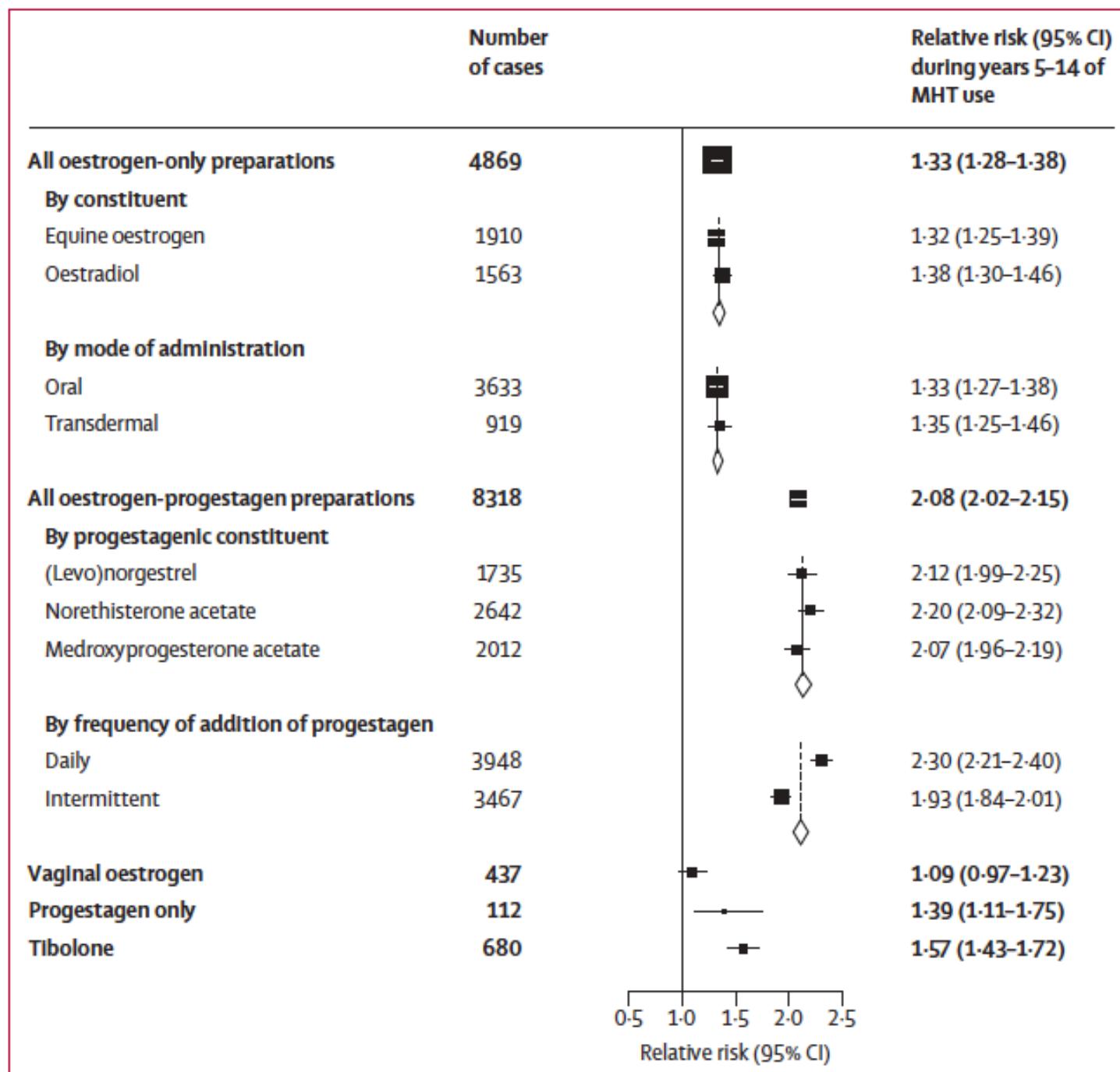


Figure 4: Main types of MHT: relative risks during years 5–14 of current use

Hormone Therapy and Venous Thromboembolism Among Postmenopausal Women: Impact of the Route of Estrogen Administration and Progestogens: The ESTHER Study

Marianne Canonico, Emmanuel Oger, Geneviève Plu-Bureau, Jacqueline Conard, Guy Meyer, Hervé Lévesque, Nathalie Trillot, Marie-Thérèse Barrellier, Denis Wahl, Joseph Emmerich, Pierre-Yves Scarabin and for the Estrogen and Thromboembolism Risk (ESTHER) Study Group
Circulation 2007;115;840-845

TABLE 2. Impact of Hormone Therapy on VTE Risk by Route of Estrogen Administration and Type of Progestogens

	Cases (n=259)	Controls (n=603)	Crude	Matched OR (95% CI)	
				Adjustment 1	Adjustment 2
Nonuse	146	384	1	1	1
Oral estrogen use	45	39	3.6 (1.5–8.8)	4.0 (1.6–10.1)	4.2 (1.5–11.6)
Transdermal estrogen use	67	180	0.8 (0.4–1.6)	0.8 (0.4–1.8)	0.9 (0.4–2.1)
No progestogens	14	40
Micronized progesterone	19	63	1.0 (0.4–2.3)	0.9 (0.4–2.2)	0.7 (0.3–1.9)
Pregnane derivatives	39	79	1.0 (0.4–2.3)	0.9 (0.4–2.2)	0.9 (0.4–2.3)
Norpregnane derivatives	40*	37†	3.8 (1.6–8.7)	4.0 (1.7–9.4)	3.9 (1.5–10.0)

Hormone replacement therapy and risk of venous thromboembolism in postmenopausal women: systematic review and meta-analysis

Marianne Canonico, postdoctoral research fellow;^{1,2} Geneviève Plu-Bureau, gynaecologist;^{1,3} Gordon D O Lowe, professor of vascular medicine;⁴ Pierre-Yves Scarabin, director of research (Inserm);^{1,2}

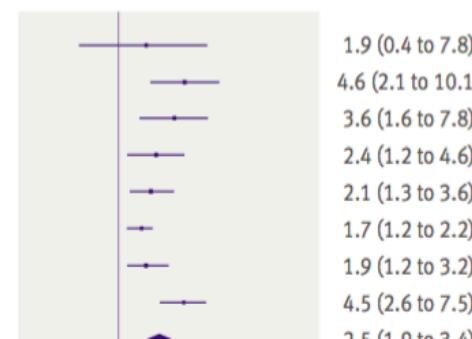
Observational studies

Oral oestrogen

- Boston CDSP 1974^{w21}
 - Daly 1996^{w1}
 - Jick 1996^{w3}
 - Nurses' health study 1996^{w4}
 - Perez-Gutthann 1997^{w5}
 - Smith 2004^{w9}
 - Douketis 2005^{w10}
 - ESTHER 2007^{w11}
 - Pooled odds ratio
- Test for homogeneity: $\chi^2=14.99$, $P=0.03$, $I^2=53.3\%$

Odds ratio
(95% CI)

Odds ratio
(95% CI)



Transdermal oestrogen

- Daly 1996^{w1}
 - Perez-Gutthann 1997^{w5}
 - Douketis 2005^{w10}
 - ESTHER 2007^{w11}
 - Pooled odds ratio
- Test for homogeneity: $\chi^2=2.92$, $P=0.40$, $I^2=0\%$



Randomised controlled trials

Oral oestrogen

- PEPI 1995^{w12}
 - HERS 1998^{w13}
 - EVTET 2000^{w14}
 - ERA 2000^{w15}
 - WEST 2001^{w16}
 - ESPRIT 2002^{w17}
 - WHI I 2002^{w18}
 - WHI II 2004^{w19}
 - WISDOM 2007^{w20}
 - Pooled odds ratio
- Test for homogeneity: $\chi^2=17.01$, $P=0.03$, $I^2=58.9\%$

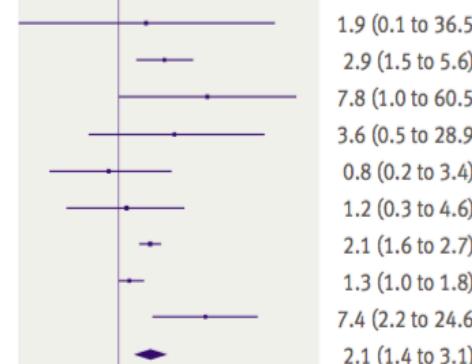


Fig 2 | Risk of first episode of venous thromboembolism by study design and route of oestrogen administration