MENOPAUSE UPDATE 2019

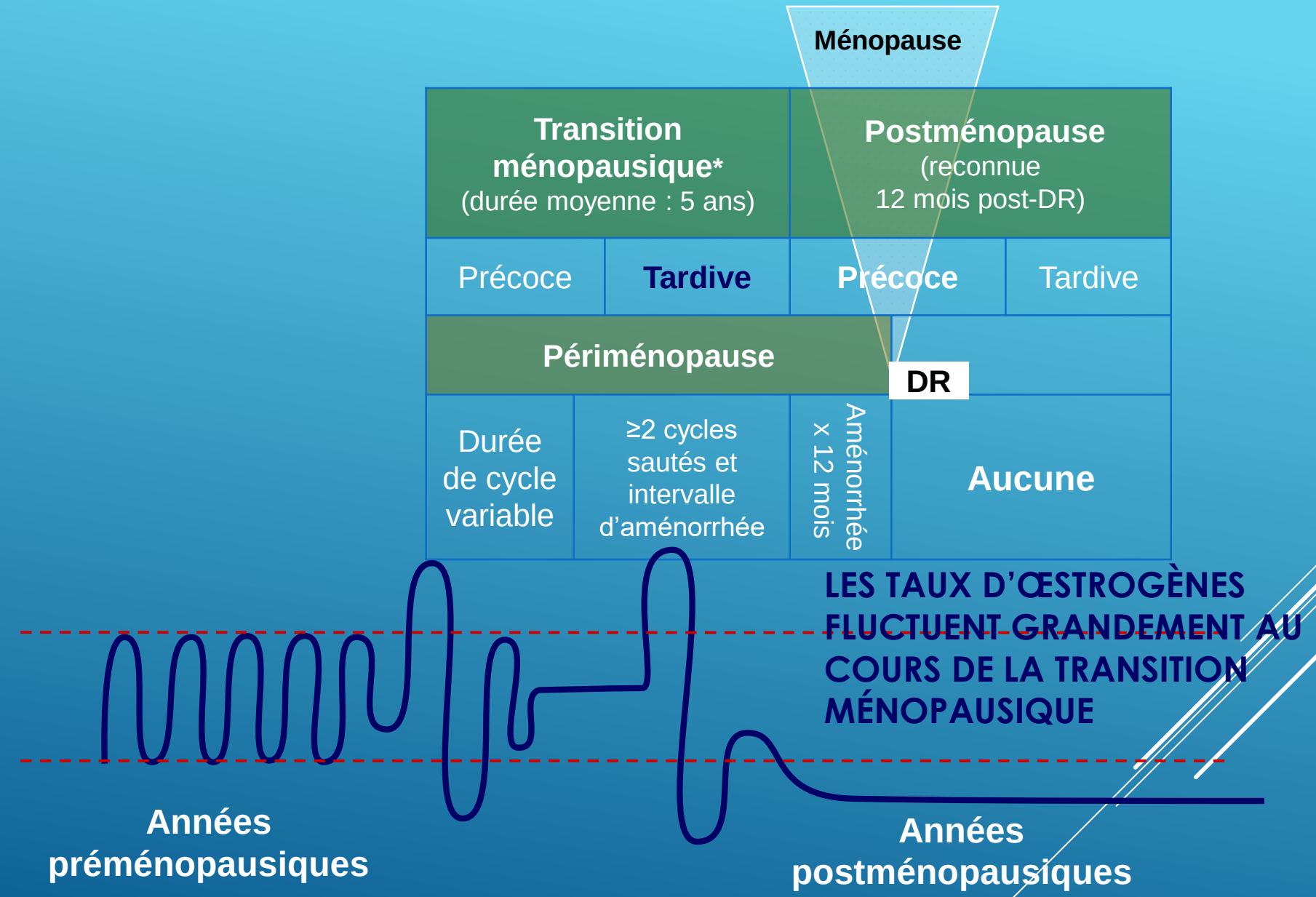
Beyond the Hot Flash
What's New in 2019

Cleve Ziegler, M.D., FRCS

CME FACULTY DISCLOSURE

Dr. Ziegler has an affiliation with the following organization that could be perceived as a real or apparent conflict of interest in the context of this presentation:

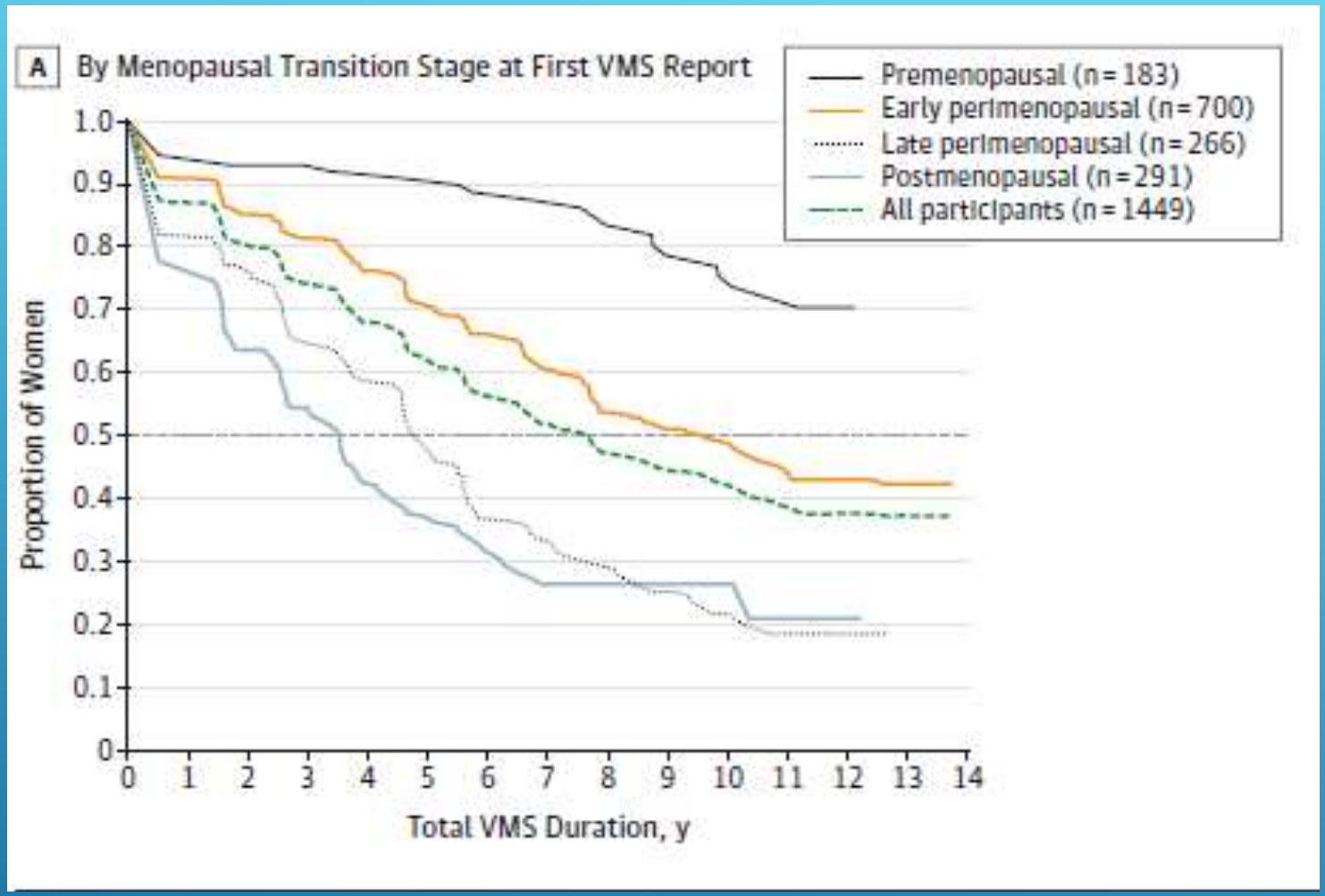
Abbvie, Allergan, Merck, Bayer, Pfizer



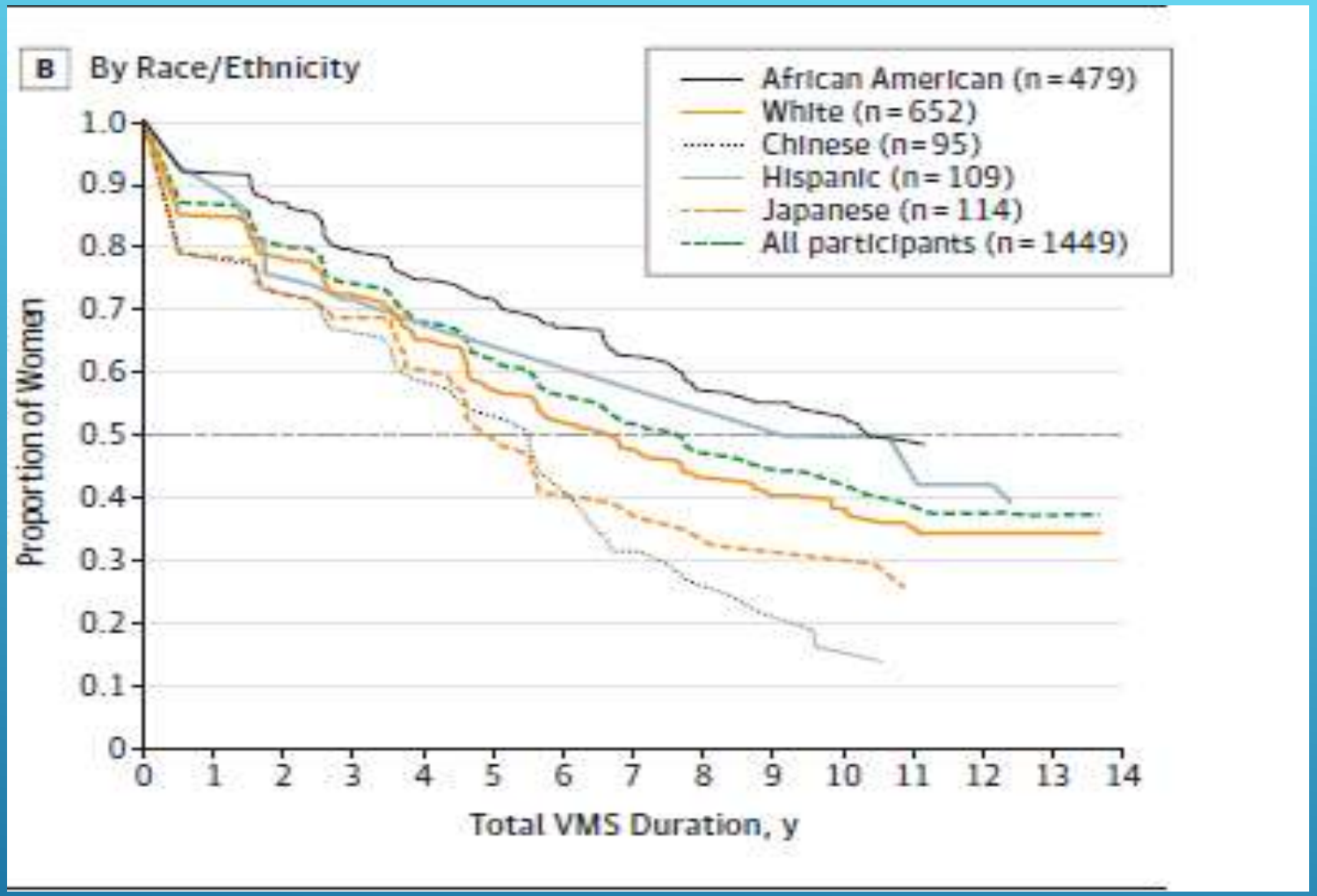
Santoro N et coll. J Clin Endocrinol Metab, vol. 81, 1996, p. 1495-1501.
Kronenberg F. Ann N Y Acad Sci, vol. 592, 1990, p. 52-86.

MENOPAUSE LINGO

- ET= Estrogen Therapy
- EPT=HRT= HT Estrogen/Progestin Therapy
- VMS= Vasomotor Symptoms
- VVA=GSM= Genitourinary Symptoms of Menopause
- WHI= Womens Health Initiative



SWAN JAMA 2015


B By Race/Ethnicity
African American (n = 479)
White (n = 652)
Chinese (n = 95)
Hispanic (n = 109)
Japanese (n = 114)
All participants (n = 1449)
Proportion of Women
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Total VMS Duration, y

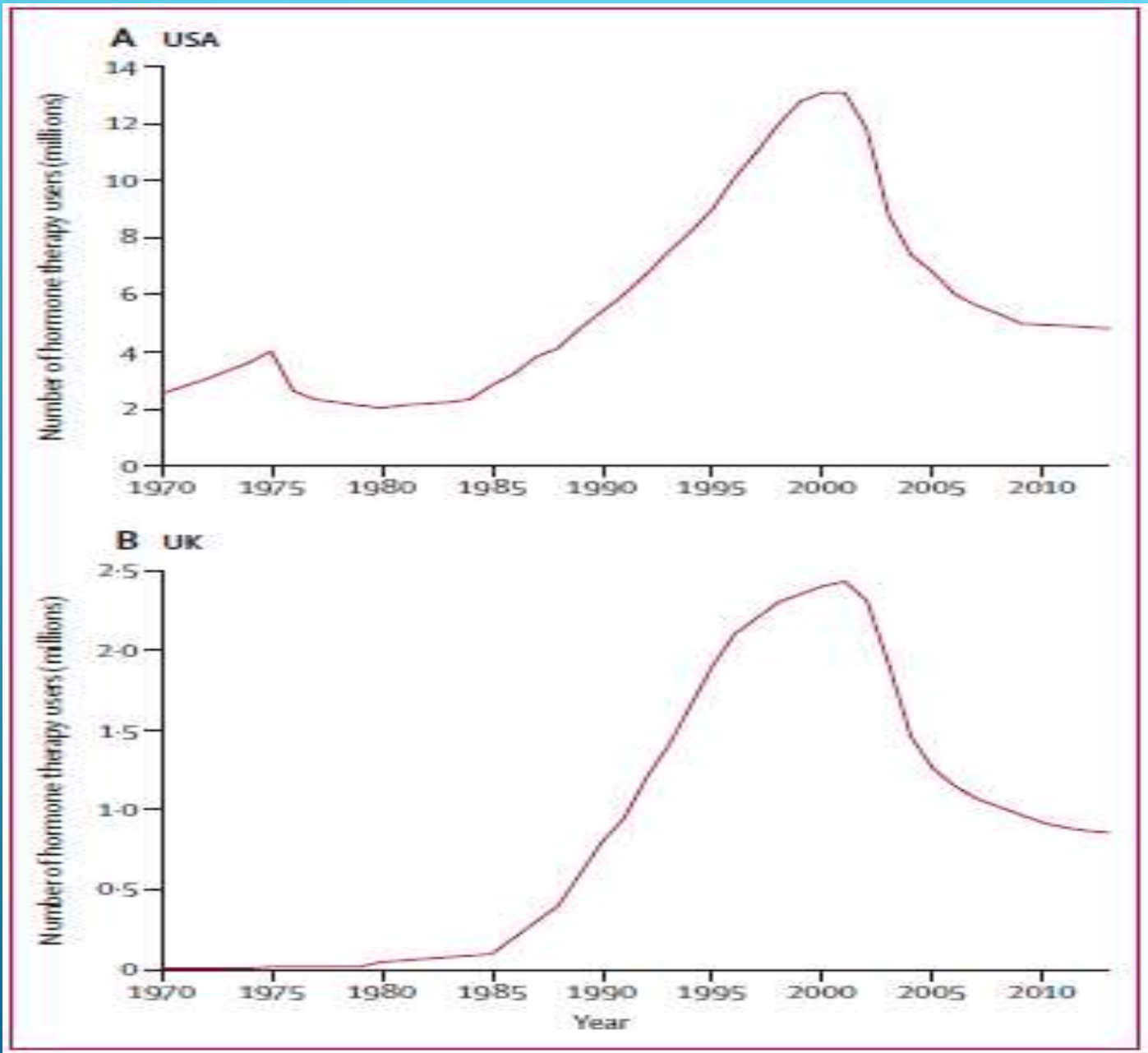
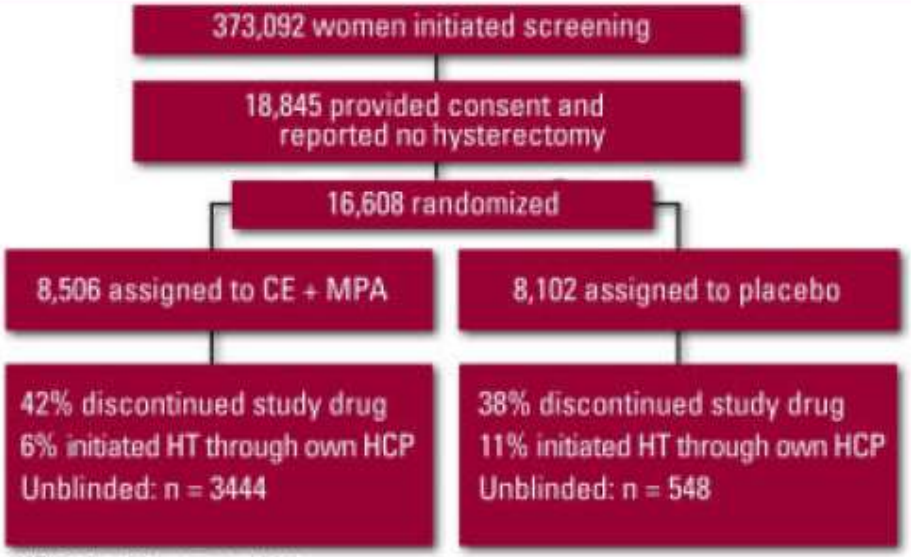


***Figure 1*: Trends in hormone therapy use in the USA and the UK since 1970**
For source of data, see appendix p 4.

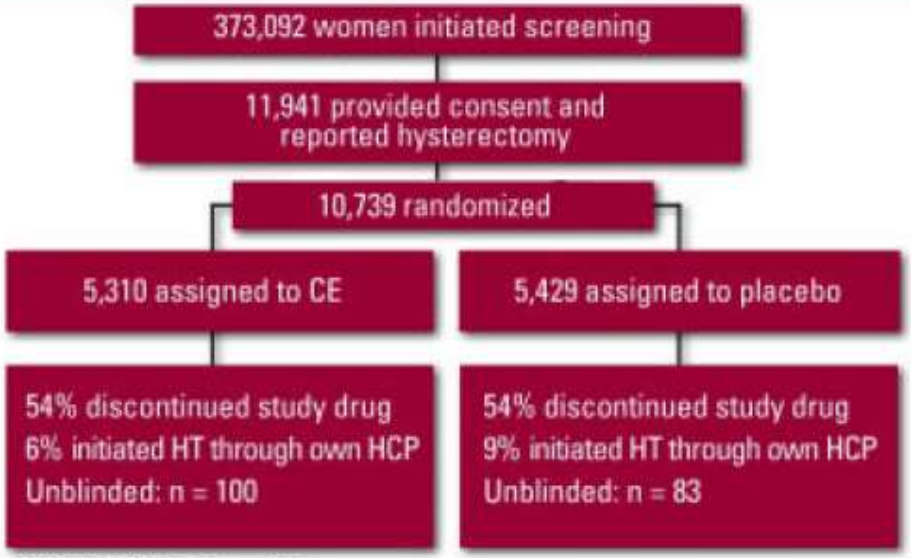
The Women's Health Initiative (WHI): Estrogen + Progestin Arm



HCP = health care provider
MPA = medroxyprogesterone acetate

Rossouw JE, et al. *JAMA* 2002;288:321

WHI: Estrogen-only Arm



HCP = health care provider
CE = conjugated estrogen

Anderson GL, et al. *JAMA* 2004;291:1701

WHI: Estrogen + Progestin Arm: Baseline Characteristics

Characteristic	CE + MPA (n = 8,506)	Placebo (n = 8,102)
Mean age at screening, y (SD)	63.2 (7.1)	63.3 (7.1)
Age group at screening, n (%)		
50–59 years	2,839 (33.4)	2,683 (33.1)
60–69 years	3,853 (45.3)	3,657 (45.1)
70–79 years	1,814 (21.3)	1,762 (21.7)
Hormone use, n (%)		
Never	6,280 (73.9)	6,024 (74.4)
Past	1,674 (19.7)	1,588 (19.6)
Current†	548 (6.4)	487 (6.0)

†Required a 3-month washout prior to randomization.

Rossouw JE, et al. *JAMA* 2002;288:321

WHI: Estrogen + Progestin Arm: Study Endpoints

Primary endpoints	Secondary endpoints
– Coronary heart disease (CHD)	– Stroke
– Breast cancer	– Pulmonary embolism
	– Hip fracture
	– Colorectal cancer
	– Endometrial cancer
	– Death

WHI: Estrogen + Progestin Arm: Alarming Results?

	RR	%
Breast cancer	1.26	+ 26%
CHD	1.29	+ 29%
Stroke	1.41	+ 41%
PE	2.13	+113%
However...		
Colorectal cancer	0.63	- 37%
Hip fracture	0.66	- 34%
Endometrial cancer	0.83	- 17%
Death from other causes	0.92	- 8%

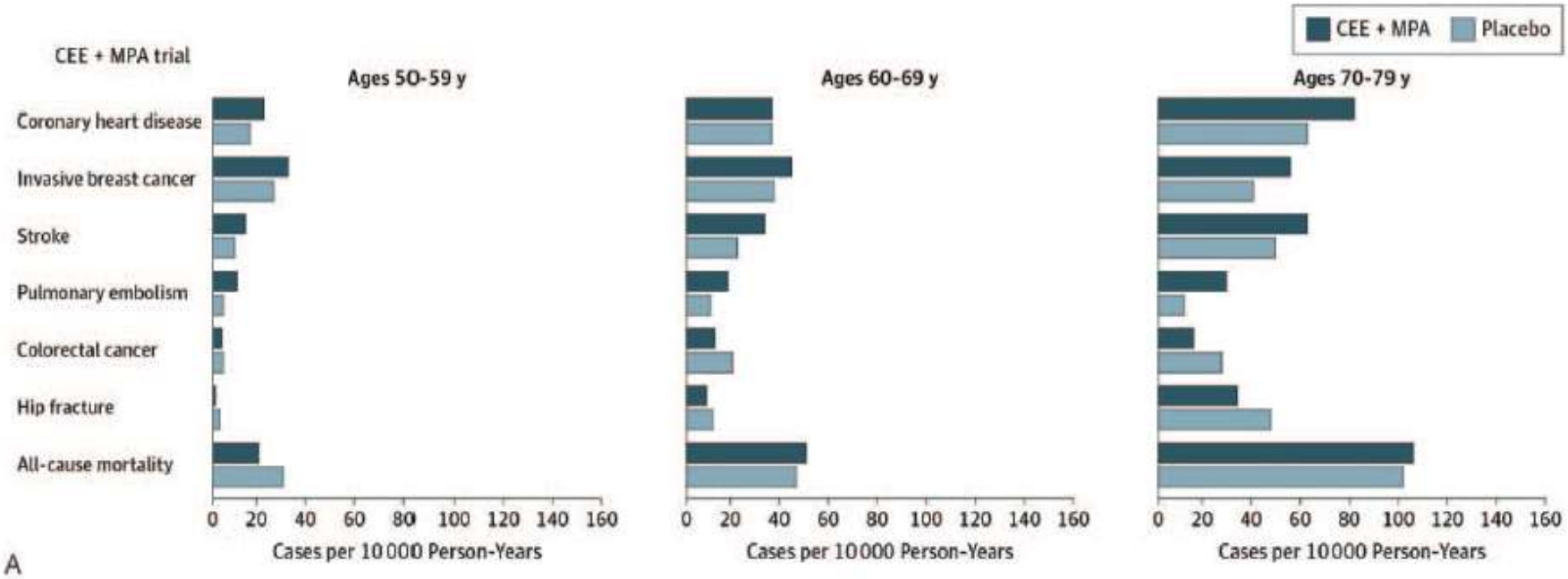
Rossouw JE, et al. *JAMA* 2002;288:321

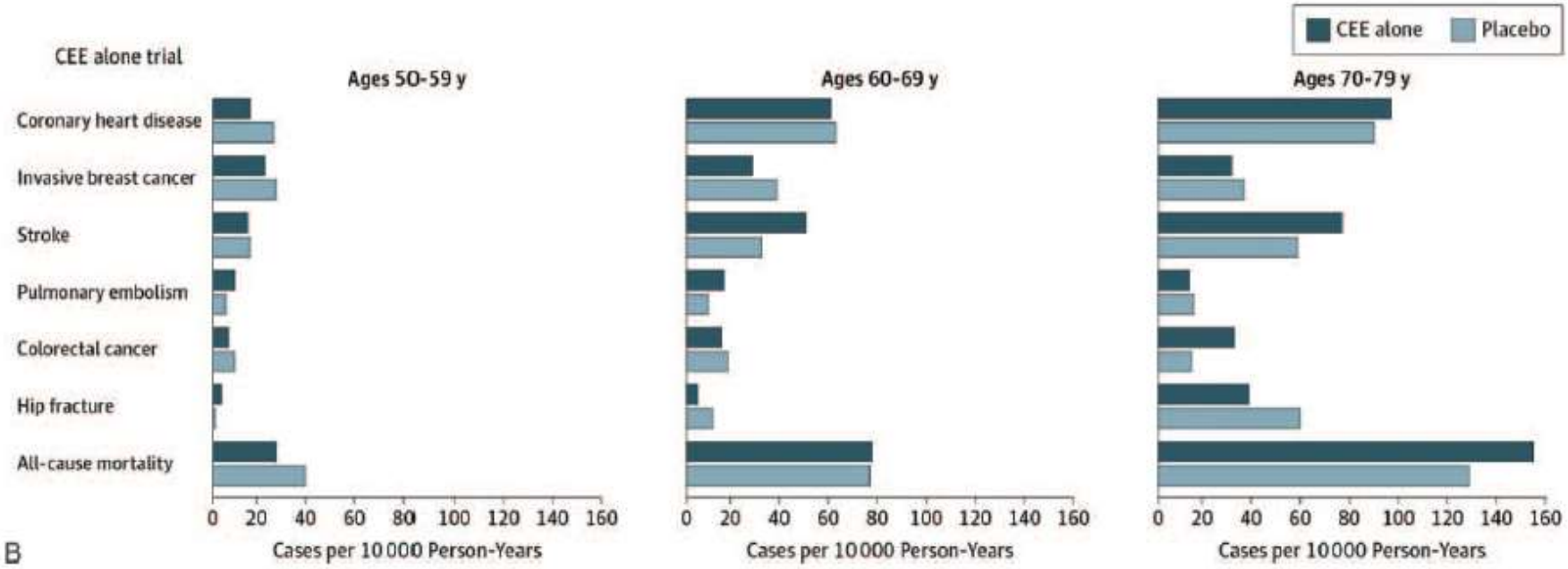
WHI Estrogen-only Results: Overall Relative and Attributable Risk

Women 50 to 79 Years of Age at Baseline

Event	Overall HR	Confidence Intervals 95% Nominal	Confidence Intervals 95% Adjusted	Attributable Risk per 10,000 Women/Year	Benefit per 10,000 Women/Year
CHD	0.91	0.75–1.12	0.72–1.15		5
Breast cancer	0.77	0.59–1.01	0.57–1.06		7
Strokes	1.39	1.10–1.77	0.97–1.99	12	
VTE	1.33	0.99–1.79	0.86–2.08	7	
PE	1.34	0.87–2.06	0.70–2.55	3	
Colorectal cancer	1.08	0.75–1.55	0.63–1.86	1	
Hip fractures	0.61	0.41–0.91	0.33–1.11		6
Total fractures	0.70	0.63–0.79	0.59–0.83		56

Anderson GL, et al. *JAMA* 2004;291:1701


CEE + MPA trial
CEE + MPA
Placebo
Ages 50-59 y
Ages 60-69 y
Ages 70-79 y
Coronary heart disease
Invasive breast cancer
Stroke
Pulmonary embolism
Colorectal cancer
Hip fracture
All-cause mortality
0 20 40 60 80 100 120 140 160
Cases per 10 000 Person-Years
A


CEE alone trial
CEE alone
Placebo
Ages 50-59 y
Ages 60-69 y
Ages 70-79 y
Coronary heart disease
Invasive breast cancer
Stroke
Pulmonary embolism
Colorectal cancer
Hip fracture
All-cause mortality
0 20 40 60 80 100 120 140 160
Cases per 10 000 Person-Years
B

Key Points

Question What is the relationship between use of menopausal hormone therapy vs placebo for 5 to 7 years and mortality over 18 years of follow-up?

Findings Among postmenopausal women who participated in 2 parallel randomized trials of estrogen plus progestin and estrogen alone, all-cause mortality rates for the overall cohort in the pooled trials were not significantly different for the hormone therapy groups vs the placebo groups (27.1% vs 27.6%; hazard ratio, 0.99 [95% CI, 0.94-1.03]).

Meaning Menopausal hormone therapy for 5 to 7 years was not associated with risk of long-term all-cause mortality.

JAMA | Original Investigation

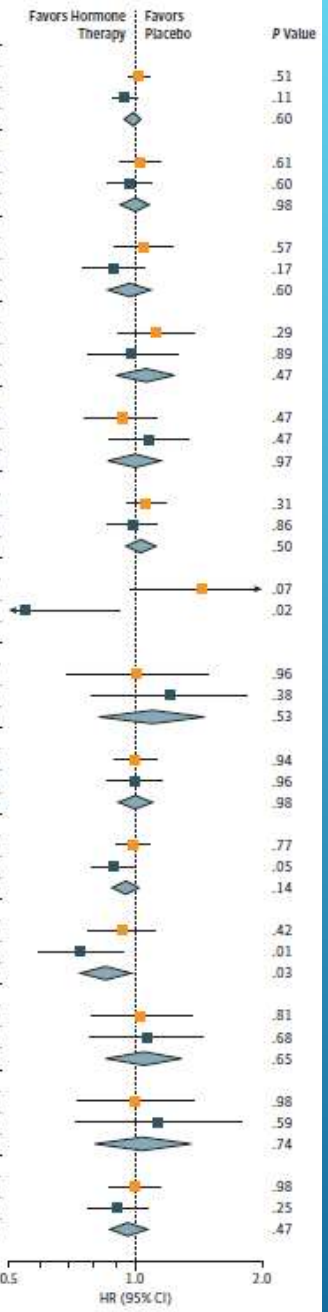
Menopausal Hormone Therapy and Long-term All-Cause and Cause-Specific Mortality

The Women's Health Initiative Randomized Trials

JAMA 2017

Figure 2. Mortality Outcomes in the Women's Health Initiative Hormone Therapy Trials During the 18-Year Cumulative Follow-up

End Points	No. of Deaths, Annualized Rates (%) Hormone Therapy	Placebo	HR (95% CI)	P Value
All-cause mortality				
CEE plus MPA vs placebo	2244 (1.58)	2110 (1.57)	1.02 (0.96-1.08)	.51
CEE alone vs placebo	1505 (1.73)	1630 (1.83)	0.94 (0.88-1.01)	.11
Pooled trials			0.99 (0.94-1.03)	.60
CVD mortality[a]				
CEE plus MPA vs placebo	688 (0.49)	644 (0.48)	1.03 (0.92-1.15)	.61
CEE alone vs placebo	547 (0.63)	577 (0.65)	0.97 (0.86-1.09)	.60
Pooled trials			1.00 (0.92-1.08)	.98
CHD mortality				
CEE plus MPA vs placebo	310 (0.22)	285 (0.21)	1.05 (0.89-1.23)	.57
CEE alone vs placebo	240 (0.28)	277 (0.31)	0.89 (0.75-1.05)	.17
Pooled trials			0.97 (0.86-1.09)	.60
Stroke mortality				
CEE plus MPA vs placebo	188 (0.13)	161 (0.12)	1.12 (0.91-1.38)	.29
CEE alone vs placebo	126 (0.14)	132 (0.15)	0.98 (0.77-1.26)	.89
Pooled trials			1.06 (0.90-1.24)	.47
Other known CVD mortality				
CEE plus MPA vs placebo	188 (0.13)	195 (0.14)	0.93 (0.76-1.13)	.47
CEE alone vs placebo	174 (0.20)	164 (0.18)	1.08 (0.87-1.34)	.47
Pooled trials			1.00 (0.86-1.15)	.97
Cancer mortality				
CEE plus MPA vs placebo	706 (0.50)	638 (0.47)	1.06 (0.95-1.18)	.31
CEE alone vs placebo	424 (0.49)	439 (0.49)	0.99 (0.86-1.13)	.86
Pooled trials			1.03 (0.95-1.12)	.50
Breast cancer mortality				
CEE plus MPA vs placebo	61 (0.043)	40 (0.030)	1.44 (0.97-2.15)	.07
CEE alone vs placebo	22 (0.025)	41 (0.046)	0.55 (0.33-0.92)	.02
Pooled trials			NR[b]	
Colorectal cancer mortality				
CEE plus MPA vs placebo	53 (0.037)	50 (0.037)	1.01 (0.69-1.49)	.96
CEE alone vs placebo	47 (0.054)	40 (0.045)	1.21 (0.79-1.84)	.38
Pooled trials			1.10 (0.82-1.46)	.53
Other known cancer mortality				
CEE plus MPA vs placebo	548 (0.39)	521 (0.39)	1.00 (0.89-1.13)	.94
CEE alone vs placebo	336 (0.39)	345 (0.39)	1.00 (0.86-1.16)	.96
Pooled trials			1.00 (0.91-1.10)	.98
Other mortality				
CEE plus MPA vs placebo	850 (0.60)	828 (0.61)	0.99 (0.90-1.08)	.77
CEE alone vs placebo	534 (0.61)	614 (0.69)	0.89 (0.79-1.00)	.05
Pooled trials			0.95 (0.88-1.02)	.14
Alzheimer's or dementia mortality				
CEE plus MPA vs placebo	223 (0.16)	233 (0.17)	0.93 (0.77-1.11)	.42
CEE alone	127 (0.15)	175 (0.20)	0.74 (0.59-0.94)	.01
Pooled trials			0.85 (0.74-0.98)	.03
COPD mortality				
CEE plus MPA vs placebo	108 (0.076)	100 (0.074)	1.03 (0.79-1.36)	.81
CEE alone vs placebo	83 (0.095)	79 (0.088)	1.07 (0.78-1.45)	.68
Pooled trials			1.05 (0.85-1.29)	.65
Accident or injury mortality				
CEE plus MPA vs placebo	78 (0.055)	74 (0.055)	1.00 (0.73-1.38)	.98
CEE alone vs placebo	39 (0.045)	35 (0.039)	1.13 (0.72-1.79)	.59
Pooled trials			1.04 (0.80-1.36)	.74
Other known mortality[c]				
CEE plus MPA vs placebo	428 (0.30)	409 (0.30)	1.00 (0.87-1.15)	.98
CEE alone vs placebo	277 (0.32)	313 (0.35)	0.91 (0.77-1.07)	.25
Pooled trials			0.96 (0.87-1.07)	.47



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**

Summary

Background Published findings on breast cancer risk associated with different types of menopausal hormone therapy (MHT) are inconsistent, with limited information on long-term effects. We bring together the epidemiological evidence, published and unpublished, on these associations, and review the relevant randomised evidence.

Methods Principal analyses used individual participant data from all eligible prospective studies that had sought information on the type and timing of MHT use; the main analyses are of individuals with complete information on this. Studies were identified by searching many formal and informal sources regularly from Jan 1, 1992, to Jan 1, 2018. Current users were included up to 5 years (mean 1·4 years) after last-reported MHT use. Logistic regression yielded adjusted risk ratios (RRs) comparing particular groups of MHT users versus never users.

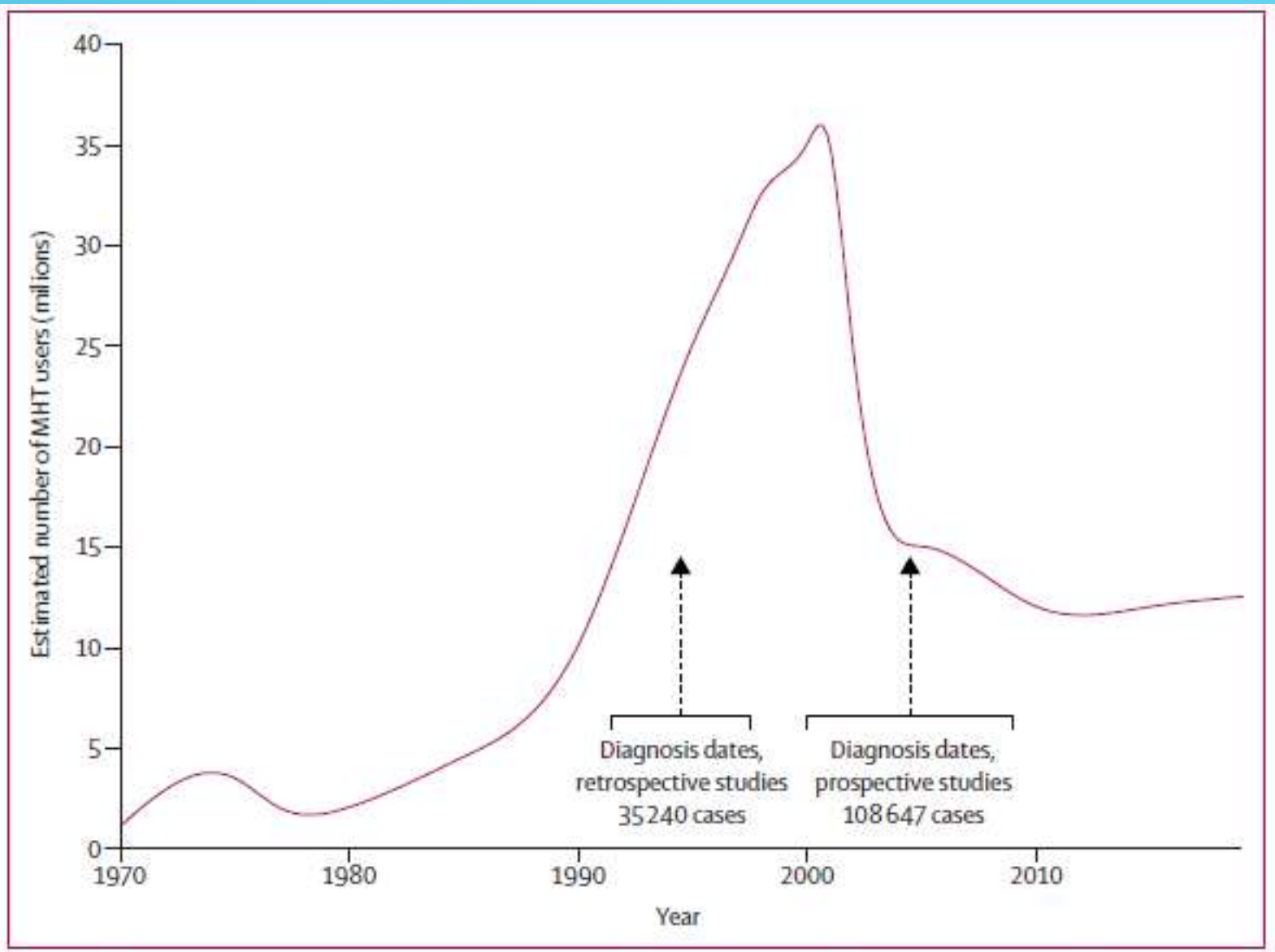


Figure 1: **Estimated number of current MHT users in western countries in the 50 years since 1970, and the distribution of the dates of diagnosis of breast cancer in the retrospective and the prospective studies**
Vertical lines give median dates of diagnosis, and horizontal lines give IQRs. MHT=menopausal hormone therapy.

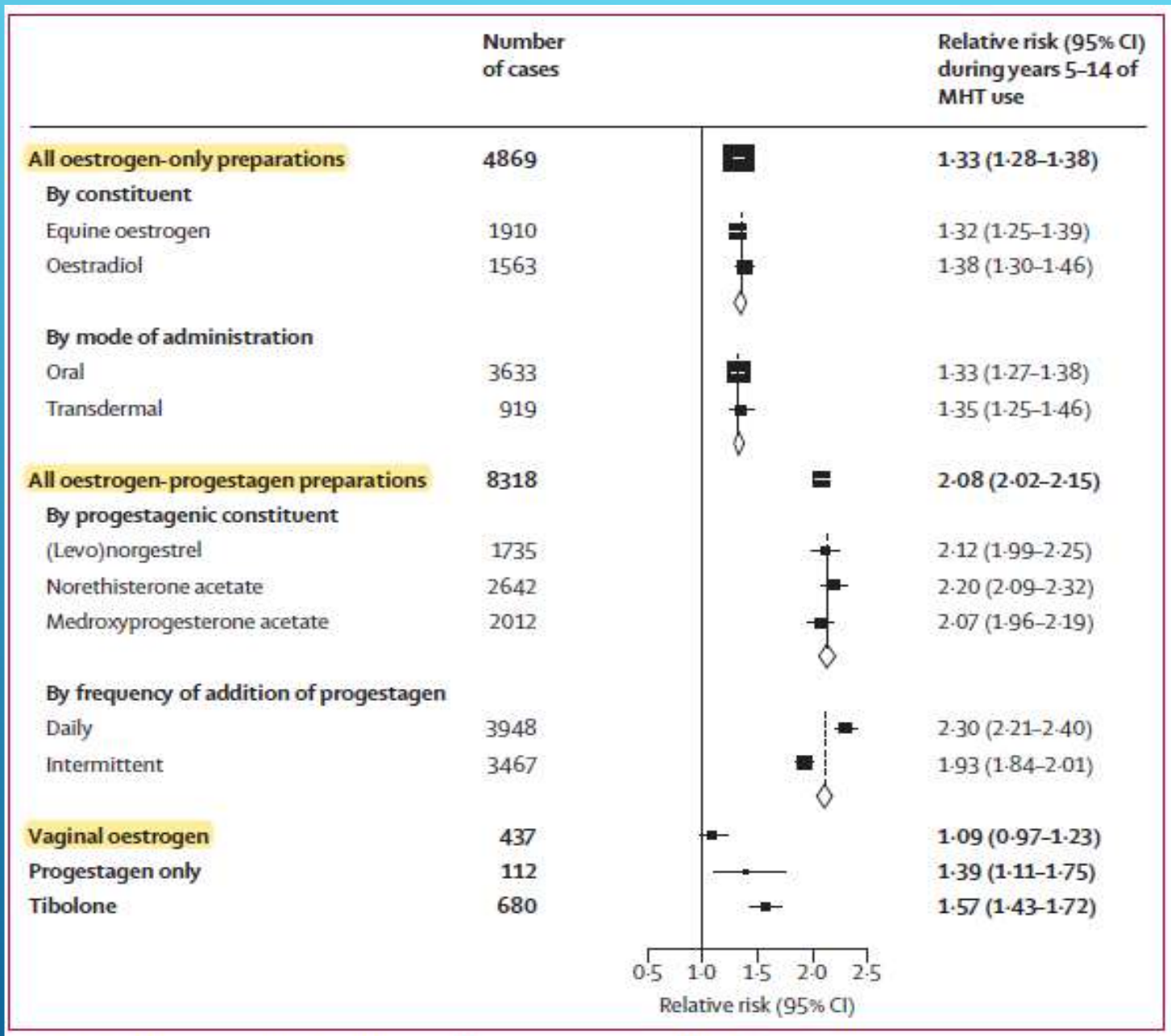


Figure 4: Main types of MHT: relative risks during years 5–14 of current use

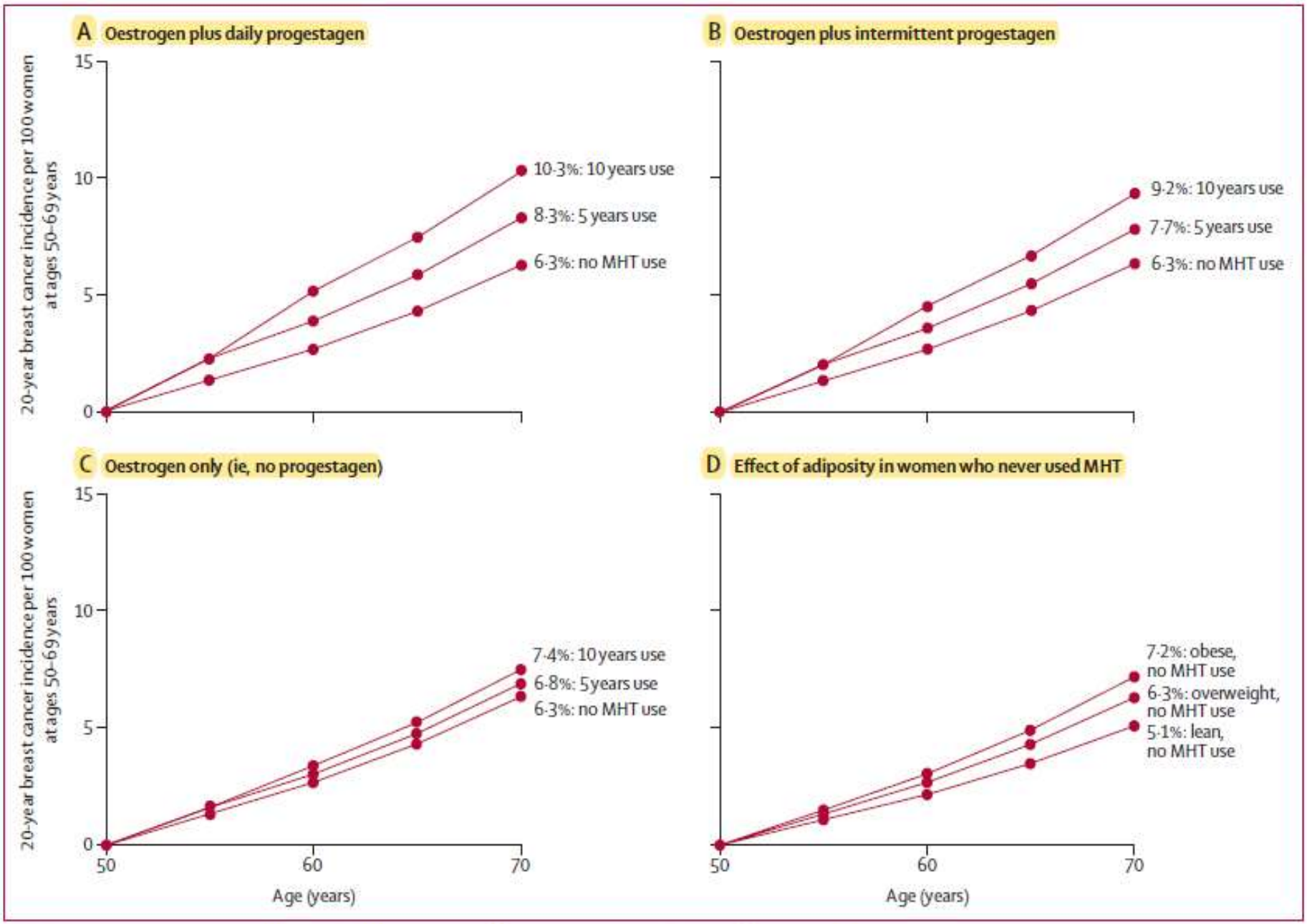


Figure 7: Effect of 5 years or of 10 years of MHT use, starting from age 50 years, on 20-year breast cancer incidence rates

Implications of all the available evidence

If the associations are largely causal, MHT use in western countries has already caused about 1 million breast cancers, out of a total of about 20 million since 1990. For women of average weight in western countries, 5 years use of oestrogen plus daily progestagen MHT, starting at age 50 years, would increase 20-year breast cancer risks at ages 50–69 years from 6·3% to 8·3%, an absolute increase of 2·0 per 100 women (one in every 50 users). Similarly, 5 years use of oestrogen plus intermittent progestagen MHT would increase the 20-year risk from 6·3% to 7·7%, an absolute increase of 1·4 per 100 women (one in 70 users). Finally, 5 years use of oestrogen-only MHT would increase the 20-year risk from 6·3% to 6·8%, an absolute increase of 0·5 per 100 women (one in 200 users); this excess would be greater in lean women, but in obese women oestrogen-only MHT is associated with little excess risk. For 10 years of use, the 20-year increases in incidence would be about twice as great as for 5 years of use.

OPEN ACCESS

Check for updates

Use of postmenopausal hormone therapy and risk of Alzheimer's disease in Finland: nationwide case-control study

Hanna Savolainen-Peltonen,[1,2] Päivi Rahkola-Soisalo,[1] Fabian Hoti,[3] Pia Vattulainen,[3] Mika Gissler,[4,5,6] Olavi Ylikorkala,[1] Tomi S Mikkola[1,2]

WHAT IS ALREADY KNOWN ON THIS TOPIC

Data on the association between use of postmenopausal hormone therapy and risk of Alzheimer's disease are conflicting

Several observational studies have indicated that hormone therapy might have a protective effect on the risk of Alzheimer's disease, but this was not supported by the placebo controlled Women's Health Initiative Memory Study

These findings were later challenged by the timing hypothesis, which indicates that oestrogen could be neuroprotective only if it is started soon after the onset of menopause

WHAT THIS STUDY ADDS

Use of postmenopausal systemic hormone therapy is accompanied with an increase in the risk of Alzheimer's disease in postmenopausal women, whereas the use of vaginal estradiol shows no such risk

Particularly long term exposure to hormone therapy is associated with an increased risk of Alzheimer's disease, but the increase in risk is not dependent on the age at treatment initiation

Table 2 | Odds ratios for Alzheimer's disease in women younger than 60 or aged 60 and older at treatment initiation of estradiol only or various combined therapies

Age at initiation and type of hormone therapy	Patients with Alzheimer's disease (No)	Controls (No)	Odds ratio (95% CI)	P
Age <60 years				
No hormone therapy	48 331	48 925	1.00	—
Estradiol only	3125	3042	1.06 (1.01 to 1.12)	0.03
EPT	6330	5812	1.14 (1.09 to 1.19)	<0.005
EPT with MPA	1296	1247	1.08 (1.00 to 1.17)	0.06
EPT with NETA	1419	1270	1.17 (1.08 to 1.26)	<0.005
EPT with other* or mixed progestogens	3615	3295	1.15 (1.09 to 1.21)	<0.005
Tibolone	83	90	0.97 (0.72 to 1.32)	0.86
Age ≥60 years				
No hormone therapy	45 180	45 635	1.00	—
Estradiol only	1310	1157	1.15 (1.06 to 1.25)	<0.005
EPT	1630	1352	1.23 (1.14 to 1.32)	<0.005
EPT with MPA	269	227	1.21 (1.01 to 1.44)	0.04
EPT with NETA	963	792	1.23 (1.12 to 1.36)	<0.005
EPT with other* or mixed progestogens	398	333	1.21 (1.05 to 1.41)	0.009
Tibolone	90	66	1.38 (1.00 to 1.89)	0.05

EPT=oestrogen-progestogen therapy; NETA=norethisterone acetate; MPA=medroxyprogesterone acetate.
*Other progestogens include levonorgestrel, progesterone, megestrol acetate, lynestrenol, drospirenone, and trimegestone.

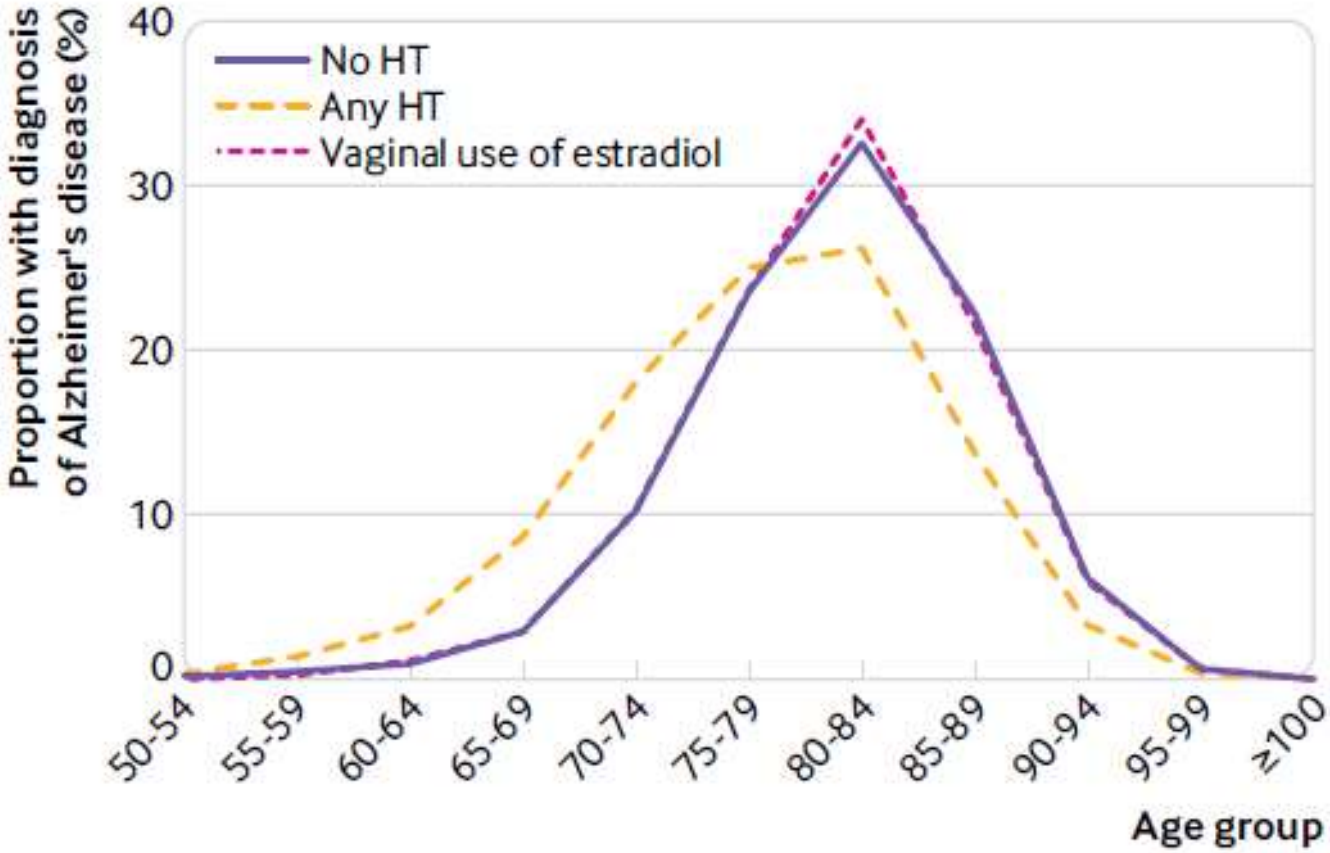


Fig 2 | Proportion (%) of women with a diagnosis of Alzheimer's disease in different age groups according to systemic use of hormone therapy, vaginal use of estradiol, or without any history of hormone therapy (HT) use

Menopause: The Journal of The North American Menopause Society
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DOI: 10.1097/GME.0000000000000921

POSITION STATEMENT

The 2017 hormone therapy position statement of The North American Menopause Society

Abstract

The 2017 Hormone Therapy Position Statement of The North American Menopause Society (NAMS) updates the 2012 Hormone Therapy Position Statement of The North American Menopause Society and identifies future research needs. An Advisory Panel of clinicians and researchers expert in the field of women's health and menopause was recruited by NAMS to review the 2012 Position Statement, evaluate new literature, assess the evidence, and reach consensus on recommendations, using the level of evidence to identify the strength of recommendations and the quality of the evidence. The Panel's recommendations were reviewed and approved by the NAMS Board of Trustees.

Hormone therapy (HT) remains the most effective treatment for vasomotor symptoms (VMS) and the genitourinary syndrome of menopause (GSM) and has been shown to prevent bone loss and fracture. The risks of HT differ depending on type, dose, duration of use, route of administration, timing of initiation, and whether a progestogen is used. Treatment should be individualized to identify the most appropriate HT type, dose, formulation, route of administration, and duration of use, using the best available evidence to maximize benefits and minimize risks, with periodic reevaluation of the benefits and risks of continuing or discontinuing HT.

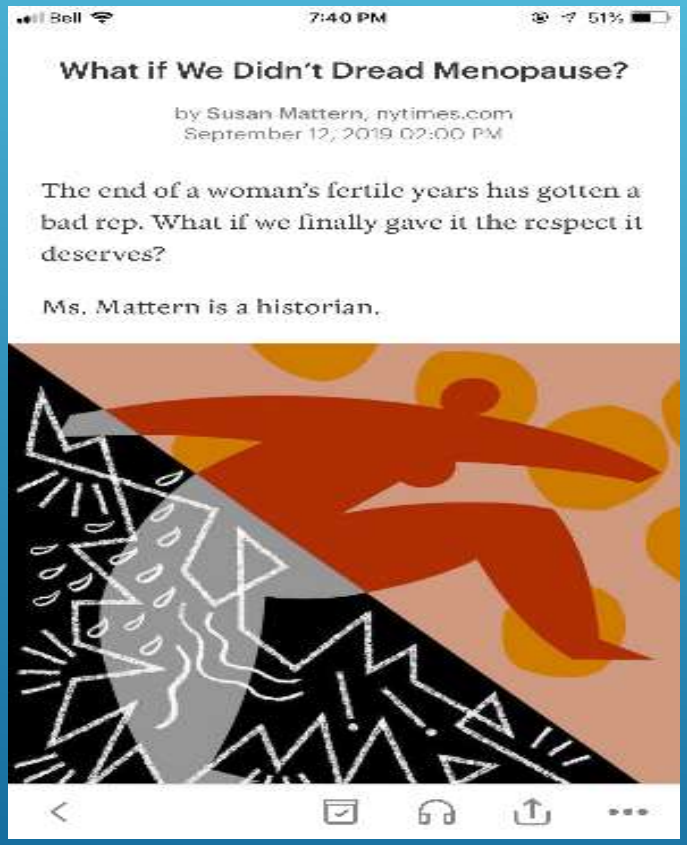
For women aged younger than 60 years or who are within 10 years of menopause onset and have no contraindications, the benefit-risk ratio is most favorable for treatment of bothersome VMS and for those at elevated risk for bone loss or fracture. For women who initiate HT more than 10 or 20 years from menopause onset or are aged 60 years or older, the benefit-risk ratio appears less favorable because of the greater absolute risks of coronary heart disease, stroke, venous thromboembolism, and dementia. Longer durations of therapy should be for documented indications such as persistent VMS or bone loss, with shared decision making and periodic reevaluation. For bothersome GSM symptoms not relieved with over-the-counter therapies and without indications for use of systemic HT, low-dose vaginal estrogen therapy or other therapies are recommended.

- Systemic HT, with estrogen alone or in combination with progestin, is the most effective therapy for vasomotor symptoms related to menopause.

- Common sense lifestyle solutions such as layering of clothing, maintaining a lower ambient temperature, and consuming cool drinks are reasonable measures for the management of vasomotor symptoms.

LIFESTYLE MODIFICATIONS

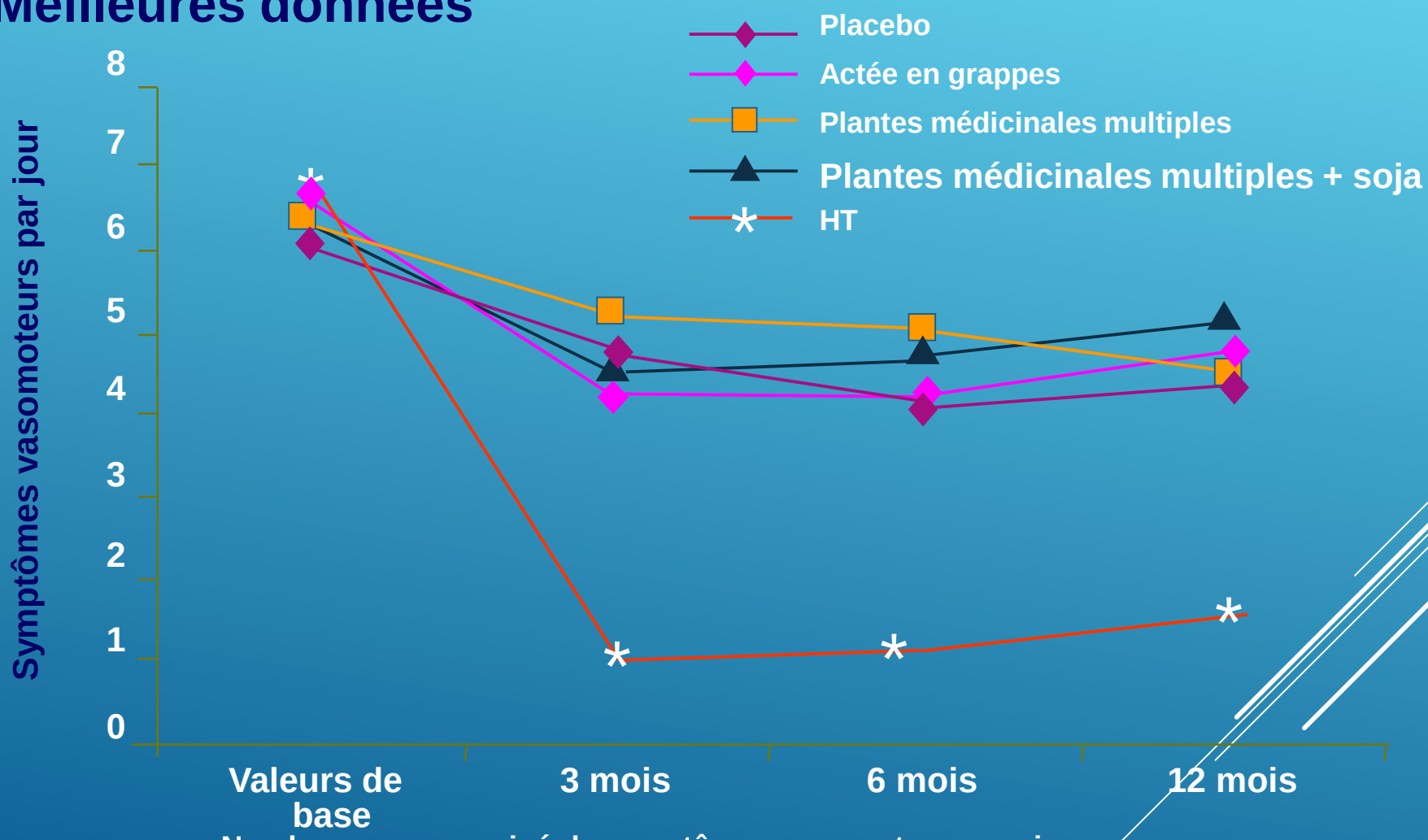
ALTERNATIVE TREATMENTS?



- Data do not show that phytoestrogens, herbal supplements, and lifestyle modifications are efficacious for the treatment of vasomotor symptoms.

Soja et phytothérapie

Meilleures données



Nombre moyen corrigé de symptômes vasomoteurs par jour, par groupe d'étude

Newton KM et coll. Ann Intern Med, vol. 145, 2006, p. 869-79. Reproduit avec permission.


Metagenics
Estrovera
DIETARY SUPPLEMENT
30


NPN 80052631
Femarelle®
For the Relief of Menopausal Symptoms and to Support Bone Health
Pour le soulagement des symptômes de la ménopause et pour soutenir la santé osseuse
28 capsules

NON RX

- Selective serotonin reuptake inhibitors, SSNRIs, clonidine, and the gabapentin are effective alternatives to HT for the treatment of vasomotor symptoms related to menopause.

- Paroxetine is the only nonhormonal therapy that is approved by the FDA for the treatment of vasomotor symptoms.

- Nonestrogen water-based or silicone-based vaginal lubricants and moisturizers may alleviate vaginal symptoms related to menopause.

- First-line therapies for women with symptomatic VVA include nonhormonal lubricants with intercourse and, if indicated, regular use of long-acting vaginal moisturizers. [Level A]

- Estrogen therapy effectively alleviates atrophic vaginal symptoms related to menopause. Local therapy is advised for the treatment of women with only vaginal symptoms.

Sécheresse vaginale : Soulagement des symptômes

Huile douce ou vitamine E

- Massée dans les tissus

Lubrifiants

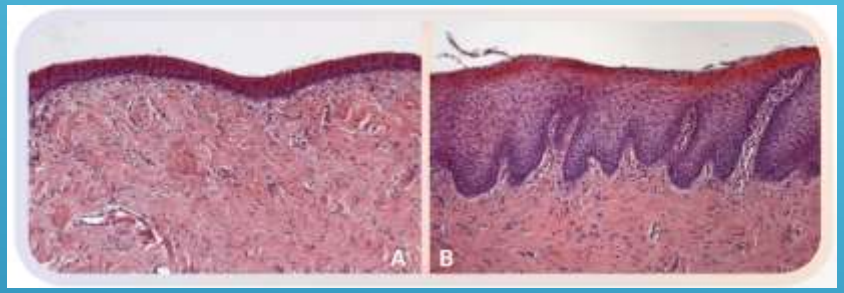
- Pendant le coït

Hydratants vaginaux

- Adhèrent au vagin

NON HORMONAL PRODUCTS

SOMETHING NEW?



LASER "REJUVENATION"

- Estrogen therapy effectively alleviates atrophic vaginal symptoms related to menopause. Local therapy is advised for the treatment of women with only vaginal symptoms.

- ET is the most effective treatment of symptoms of vulvar and vaginal atrophy; low-dose, local vaginal ET is advised when only vaginal symptoms are present.

- Estrogen therapy carries a class effect risk of VTE. Low-dose vaginal estrogen may carry a very low risk, but there has been no report of an increased risk in the vaginal estrogen clinical trials. Data in high-risk women are lacking. [Level C]

- A progestogen is generally not indicated when low-dose vaginal estrogen is administered for symptomatic VVA. Endometrial safety data are not available for use longer than 1 year. [Level B]

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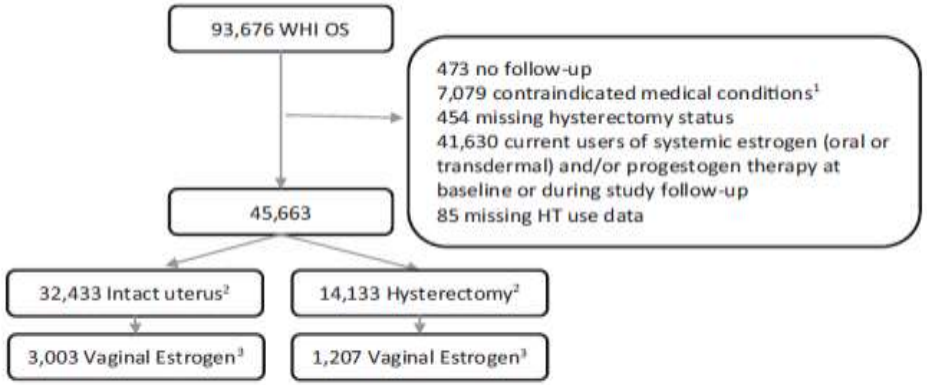
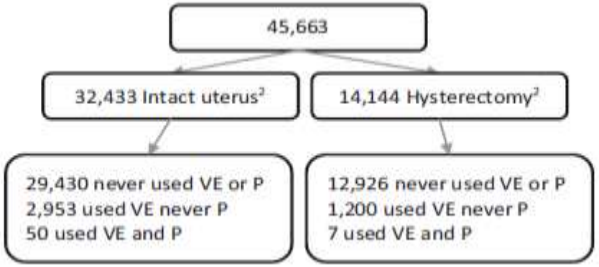
DOI: 10.1097/GME.0000000000000956

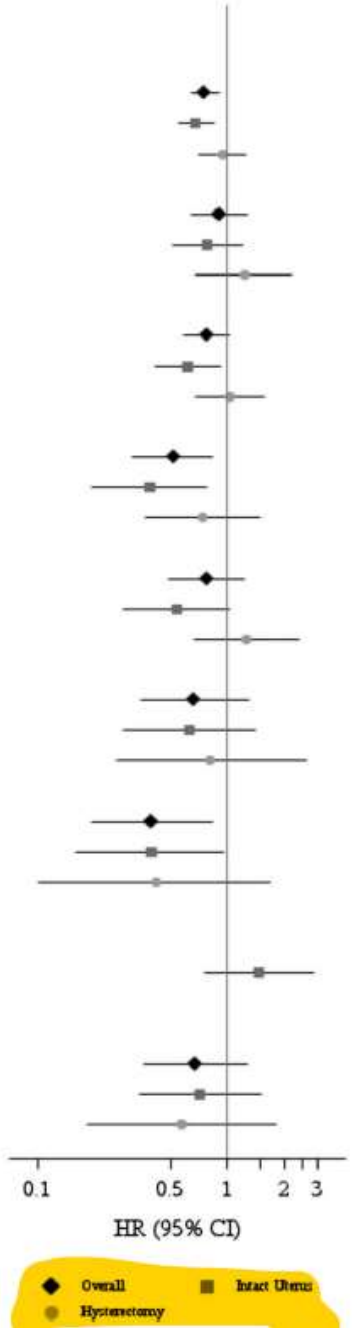
Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the Women's Health Initiative Observational Study



Participant inclusion by reported progestogen (P) use



End points	VE use N Events (rate)	No VE use N Events (rate)	HR (95% CI) Model 1	HR (95% CI) Model 2
GIE				
Overall	153 (14.0)	5906 (21.0)	0.69 (0.59, 0.81)	0.76 (0.64, 0.91)
Intact Uterus	96 (12.0)	4110 (19.9)	0.63 (0.51, 0.77)	0.68 (0.55, 0.86)
Hysterectomy	57 (19.7)	1796 (24.1)	0.83 (0.63, 1.08)	0.94 (0.70, 1.26)
Breast cancer				
Overall	40 (3.6)	1185 (4.1)	0.86 (0.62, 1.18)	0.91 (0.64, 1.29)
Intact Uterus	26 (3.2)	858 (4.0)	0.78 (0.53, 1.15)	0.79 (0.51, 1.22)
Hysterectomy	14 (4.7)	327 (4.2)	1.06 (0.61, 1.85)	1.23 (0.68, 2.21)
Death				
Overall	59 (5.3)	2592 (8.7)	0.67 (0.52, 0.87)	0.78 (0.58, 1.04)
Intact Uterus	32 (3.9)	1683 (7.7)	0.58 (0.41, 0.82)	0.62 (0.41, 0.93)
Hysterectomy	27 (9.0)	909 (11.3)	0.85 (0.58, 1.25)	1.04 (0.68, 1.58)
CHD				
Overall	20 (1.8)	1311 (4.5)	0.44 (0.29, 0.69)	0.52 (0.31, 0.85)
Intact Uterus	10 (1.2)	865 (4.0)	0.35 (0.19, 0.65)	0.39 (0.19, 0.78)
Hysterectomy	10 (3.4)	446 (5.6)	0.61 (0.33, 1.15)	0.74 (0.37, 1.50)
Stroke				
Overall	20 (1.8)	902 (3.1)	0.63 (0.40, 0.98)	0.78 (0.49, 1.24)
Intact Uterus	9 (1.1)	619 (2.9)	0.41 (0.21, 0.80)	0.54 (0.28, 1.04)
Hysterectomy	11 (3.7)	283 (3.6)	1.08 (0.59, 1.99)	1.27 (0.67, 2.40)
Colorectal cancer				
Overall	13 (1.2)	486 (1.6)	0.72 (0.41, 1.25)	0.67 (0.35, 1.31)
Intact Uterus	9 (1.1)	342 (1.6)	0.70 (0.36, 1.36)	0.63 (0.28, 1.41)
Hysterectomy	4 (1.3)	144 (1.8)	0.76 (0.28, 2.07)	0.82 (0.26, 2.62)
Hip Fracture				
Overall	10 (0.9)	582 (2.0)	0.49 (0.26, 0.92)	0.40 (0.19, 0.85)
Intact Uterus	6 (0.7)	409 (1.9)	0.42 (0.19, 0.94)	0.40 (0.16, 0.96)
Hysterectomy	4 (1.3)	173 (2.2)	0.67 (0.25, 1.81)	0.42 (0.10, 1.69)
Endometrial cancer				
Overall	NA			
Intact Uterus	11 (1.3)	222 (1.0)	1.27 (0.69, 2.33)	1.47 (0.75, 2.90)
Hysterectomy	NA			
PE/DVT				
Overall	12 (1.1)	600 (2.0)	0.59 (0.33, 1.05)	0.68 (0.36, 1.28)
Intact Uterus	9 (1.1)	385 (1.8)	0.68 (0.35, 1.31)	0.72 (0.34, 1.53)
Hysterectomy	3 (1.0)	215 (2.7)	0.43 (0.14, 1.33)	0.57 (0.18, 1.81)



Œstrogènes par voie vaginale : Nombreuses formes

Traitement efficace recommandé contre l'atrophie vulvovaginale (Résultats de catégorie A)

Crème OCE

- Applicateur
- Doigt
- Utilisation au besoin

Anneau

- Libération prolongée intravaginale
- Changer 3 fois par mois

Comprimé

- Comprimés vaginaux d'estradiol
- Insérer deux fois par semaines

Directive clinique de la SOGC : Conférence canadienne de consensus sur la ménopause, JOGC, n° 171, février 2006.

- Low-dose and ultra-low systemic doses of estrogen are associated with a better adverse effect profile than standard doses and may reduce vasomotor symptoms in some women.

- Given the variable response to HT and the associated risks, it is recommended that health care providers individualize care and treat women with the lowest effective dose for the shortest duration that is needed to relieve vasomotor symptoms.

- Both transdermal and low-dose oral estrogen have been associated with lower risks of VTE and stroke than standard doses of oral estrogen, but RCT evidence is not yet available.

- The risks of combined systemic HT include thromboembolic disease and breast cancer.

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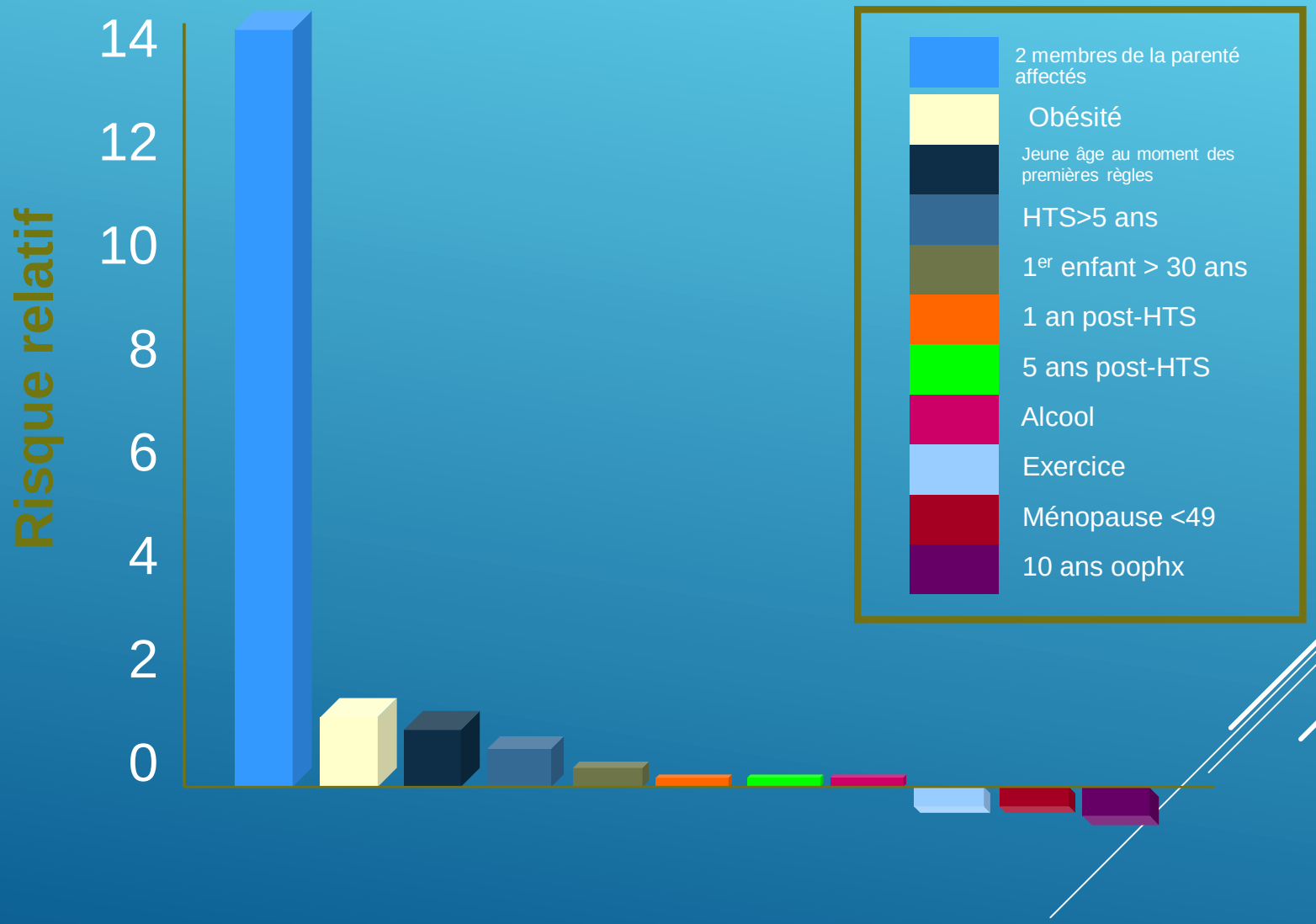
Facteurs de risque en ce qui concerne le cancer du sein

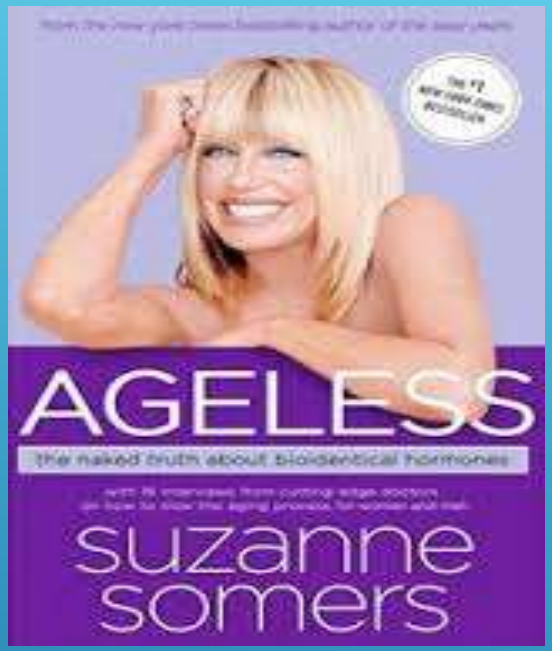



PRESCRIPTION ONLY MEDICINE
Duavive
0.45/20
0.45 mg conjugated estrogens/
20 mg bazedoxifene
modified-release tablets


HOT FLASHES
BONE LOSS
HOT FLASHES
HOT FLASHES
BONE LOSS
HOT FLASHES
HOT FLASHES
BONE LOSS
HOT FLASHES
HOT FLASHES
BONE LOSS

The following conclusions are based on limited or inconsistent scientific evidence (Level B):

- Data do not support the use of progestin-only medications, testosterone, or compounded bioidentical hormones for the treatment of vasomotor symptoms.



Association of Compounding Pharmacists of Canada

ACPC

Association des Pharmaciens Préparateurs du Canada

Your Doctor's Name_____ DEA#_____
Your Doctor's Address_____
Your Doctor's Phone Number_____
Patient's Name_____ Age_____
Address_____ Date_____

PROGESTERONE cream 25 mg/0.1 cc
Directions: Apply 0.1 cc to the labia or intravaginally daily on days 10-25 of a 28 day cycle. Dispense: 1 or 2 month supply

Refill_____ times _____
(Signature)

CONSENSUS STATEMENT

Global Consensus Position Statement on the Use of Testosterone Therapy for Women

This Position Statement has been endorsed by the International Menopause Society, The Endocrine Society, The European Menopause and Andropause Society, The International Society for Sexual Medicine, The International Society for the Study of Women's Sexual Health, The North American Menopause Society, The Federacion Latinoamericana de Sociedades de Climaterio y Menopausia, The Royal College of Obstetricians and Gynecologists, The International Society of Endocrinology, The Endocrine Society of Australia, and The Royal Australian and New Zealand College of Obstetricians and Gynecologists.* (*J Clin Endocrinol Metab* 104: 4660–4666, 2019)

(a) Testosterone therapy, *in doses that approximate physiological testosterone concentrations for premenopausal women*, exerts a beneficial effect on sexual function including increases, above the effects of placebo/comparator therapy, of an average of one satisfying sexual event per month, and increases in the subdomains of sexual desire, arousal, orgasmic function, pleasure, and sexual responsiveness, together with a reduction in sexual concerns including sexual distress (Level I, Grade A).

Summary and Key Messages

The international panel concluded the only evidence-based indication for testosterone therapy for women is for the treatment of HSDD, with available data supporting a moderate therapeutic effect. There are insufficient data to support the use of testosterone for the treatment of any other symptom or clinical condition, or for disease prevention.

- The decision to continue HT should be individualized and be based on a woman's symptoms and the risk–benefit ratio, regardless of age.

- Women with premature or early menopause who are otherwise appropriate candidates for HT can use HT at least until the median age of natural menopause (age 51 y). Longer duration of treatment can be considered if needed for symptom management.

IN SUMMARY….

- No use of HT or ET for primary or secondary prevention of disease
- Remains best choice for VMS
- Almost no contraindication to local ET
- For HT/ET, use lowest dose for shortest period of time
- Transdermal E and Natural micronized P best choice