SIPGO
Società Italiana per la Psicosomatica in Ginecologia e Ostetricia

LA MENOPAUSA COME ESPERIENZA AUTOBIOGRAFICA

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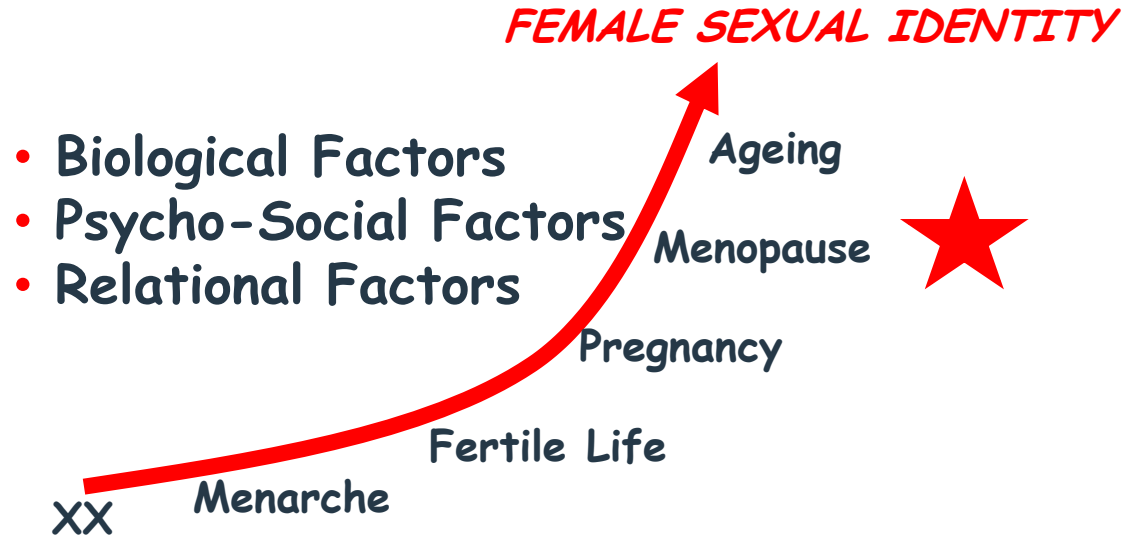
Università degli Studi di Pavia

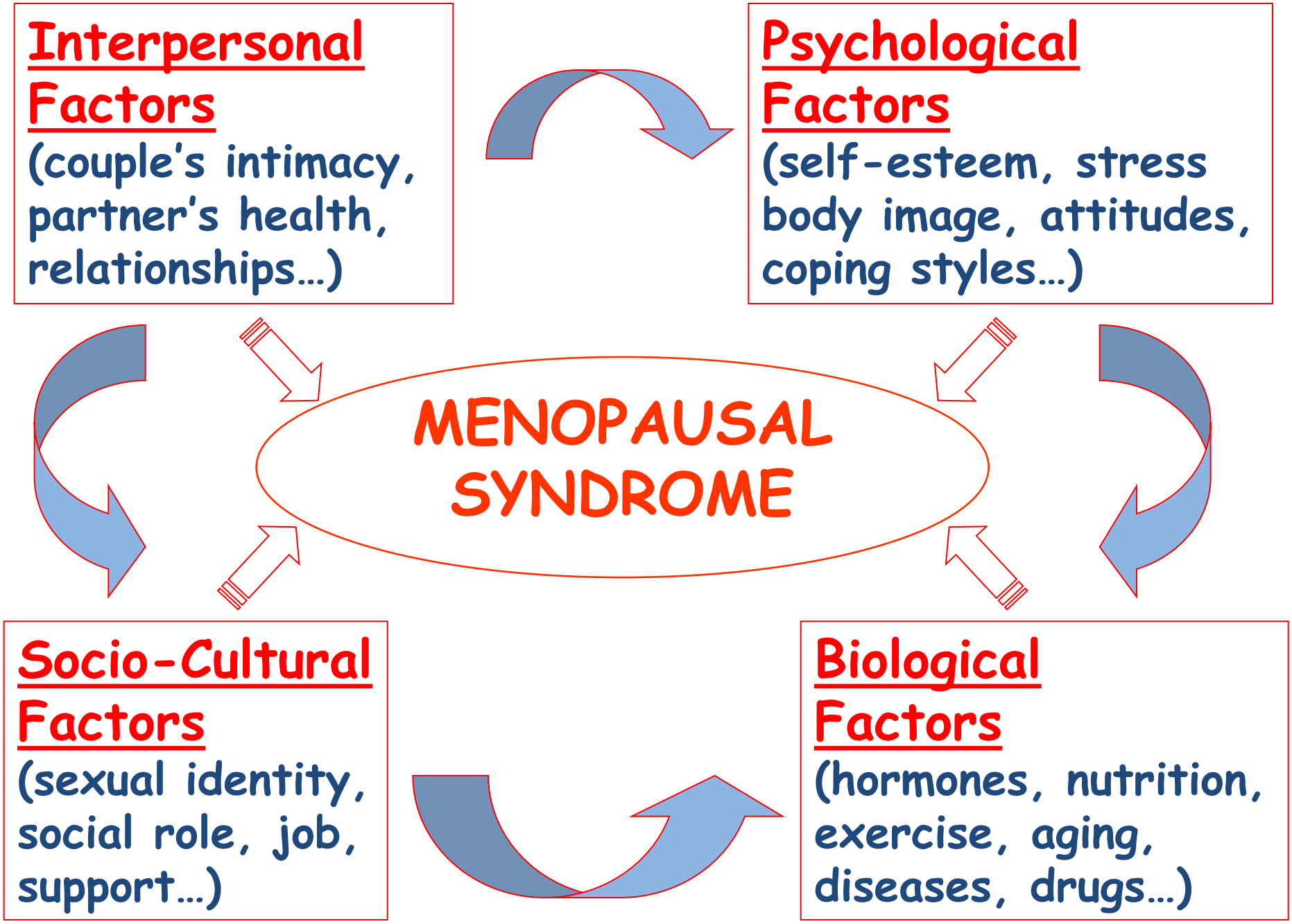
WOMEN & DOCTORS

"Discussing reproductive and sexual health with women means to meet their femininity



Dynamic and evolving concept bridging nature and nurture

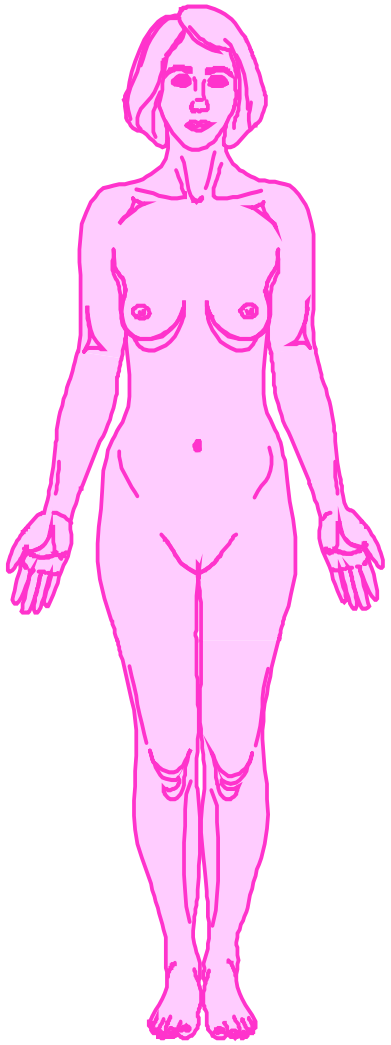
RE Nappi, 2012



RE Nappi, 2002

MENOPAUSE IS AN INDIVIDUAL EXPERIENCE

SYMPTOMS
DISEASES

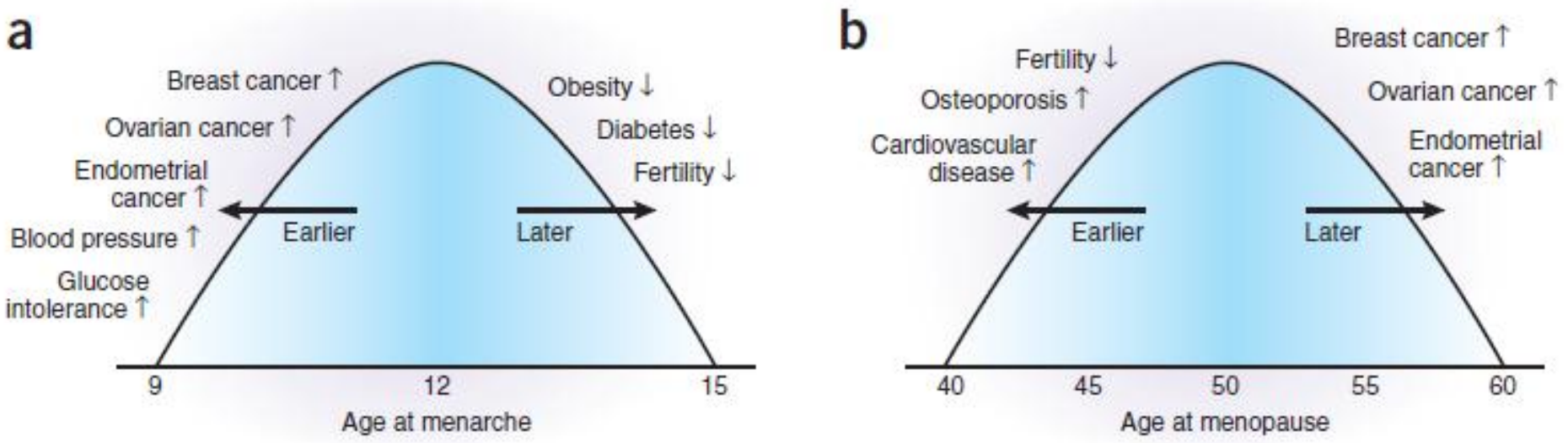


Vulnerability depends on

- GENETIC DISPOSITION
- MULTI-SYSTEM IMPLICATIONS OF SEX HORMONES CHANGES
- LIFE-STYLE AND HEALTH CARE
- PSYCHO-RELATIONAL FACTORS
- SOCIO-CULTURAL ENVIRONMENT

RE Nappi, 2013

POTENTIAL HEALTH IMPACT OF OVARIAN AGING

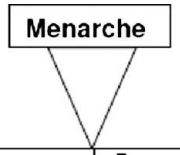


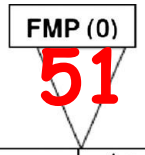
- Longer cumulative exposures to estrogen and progesterone or specific hormonal exposure during a window of susceptibility may increase or decrease some health risks
- Does a gene that influences menarche/menopause directly affect the risk of developing a disease?

HORMONES, GENES OR BOTH?

P Hartge, 2009

GLI STADI DELLA MENOPAUSA





51

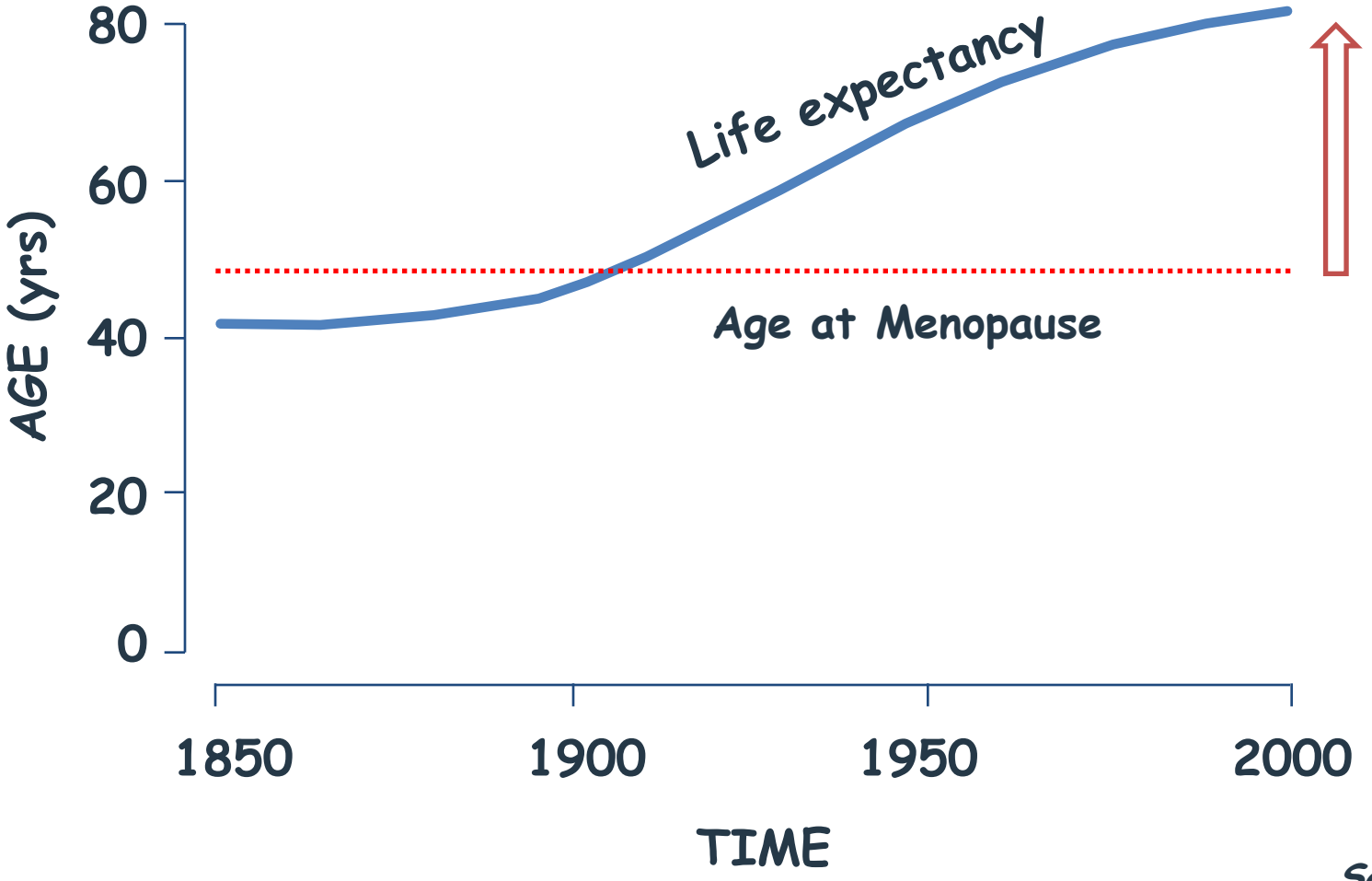
Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	*variable*				*variable*	1-3 years	2 years (1+1)		3-6 years	*Remaining lifespan*
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable to regular	Regular	Regular	Subtle changes in Flow/ Length	*Variable Length* Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of >=60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable Low Low	↑ Variable Low Low	↑ >25 IU/L** Low Low	↑ Variable Low Low		Stabilizes Very Low Very Low	
Antral Follicle Count			Low	Low	Low	**Low**	Very Low		Very Low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms *Likely*	Vasomotor symptoms *Most Likely*			*Increasing* symptoms of urogenital atrophy

* Blood draw on cycle days 2-5 ↑ = elevated

**Approximate expected level based on assays using current international pituitary standard[67-69]

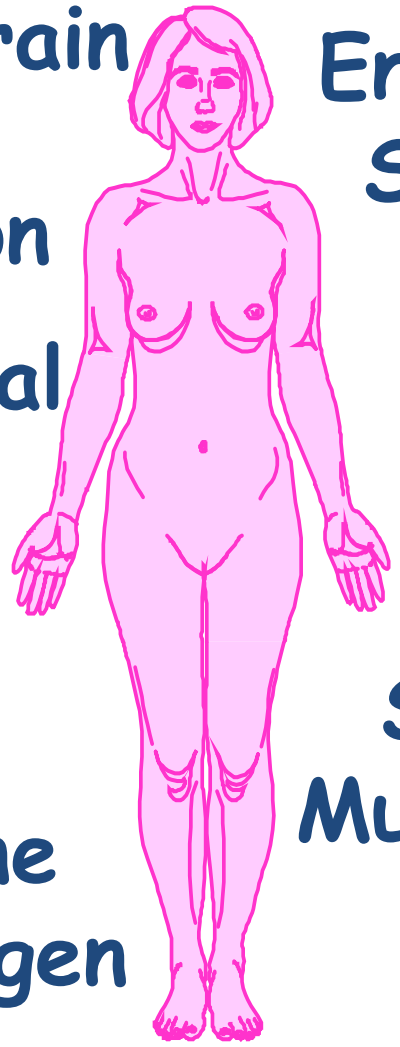
Harlow et al, 2012

MORE THAN 30 YEARS OF LIFE WITHOUT ESTROGENS



Soules, 1982

ESTROGENS & WOMEN'S HEALTH



Brain

Heart
Circulation

Gastro-Intestinal
System

Uro-Genital
Apparatus

Bone
Collagen

Endocrine
System

Breast

Immune
System

Skin
Mucosae

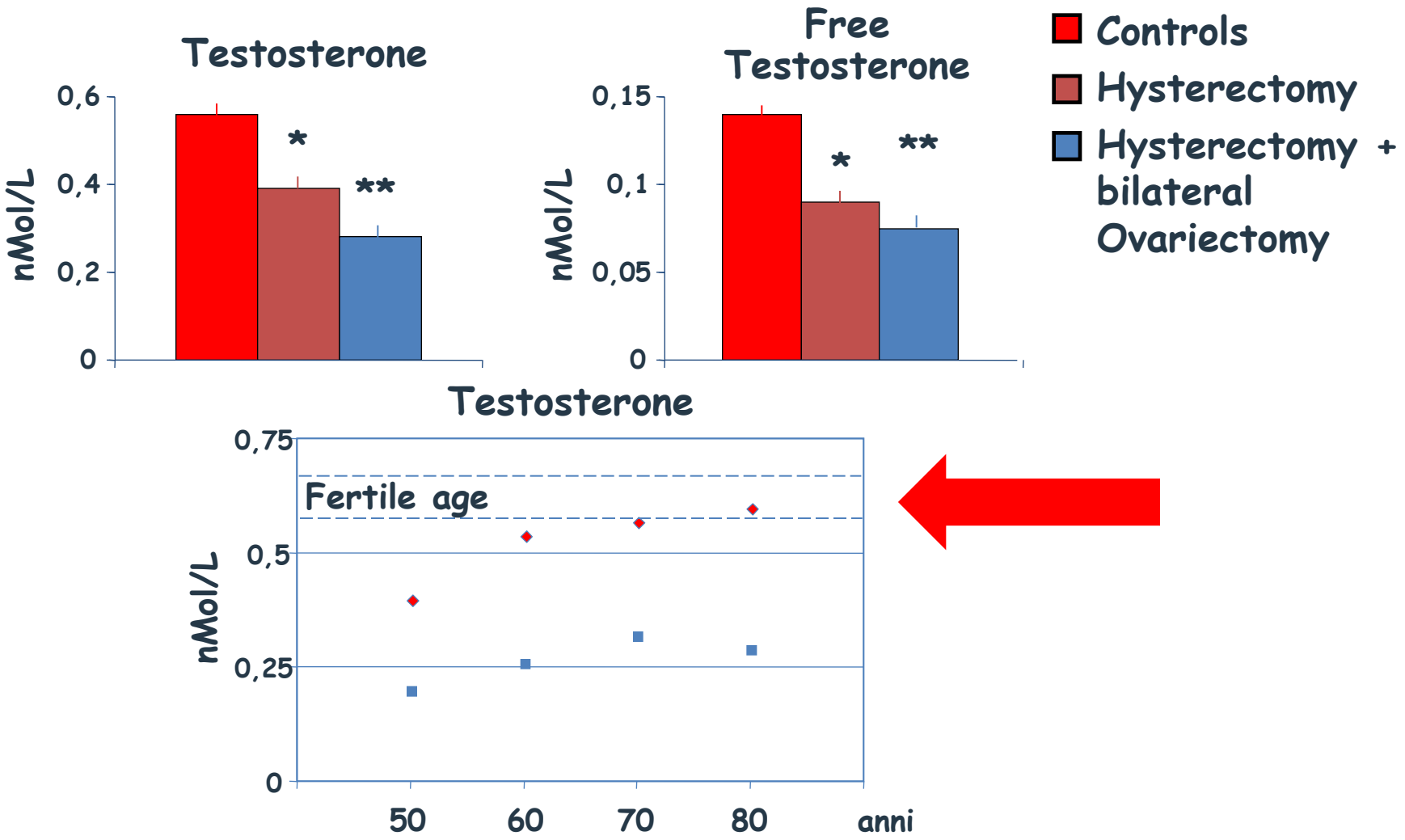
RE Nappi, 2000

SEX STEROIDS IN FERTILE AGE & MENOPAUSE

SEX HORMONES [pg/mL]	FERTILE AGE	NATURAL MENOPAUSE	SURGICAL MENOPAUSE
Estradiol	50-300	10-15	10
Progesterone	50-10.000	500	50
Testosterone	400	290	110
Androstenedione	1.900	1.000	700
DHEA	5.000	2.000	1.800
DHEAS	3.000.000	1.000.000	1.000.000

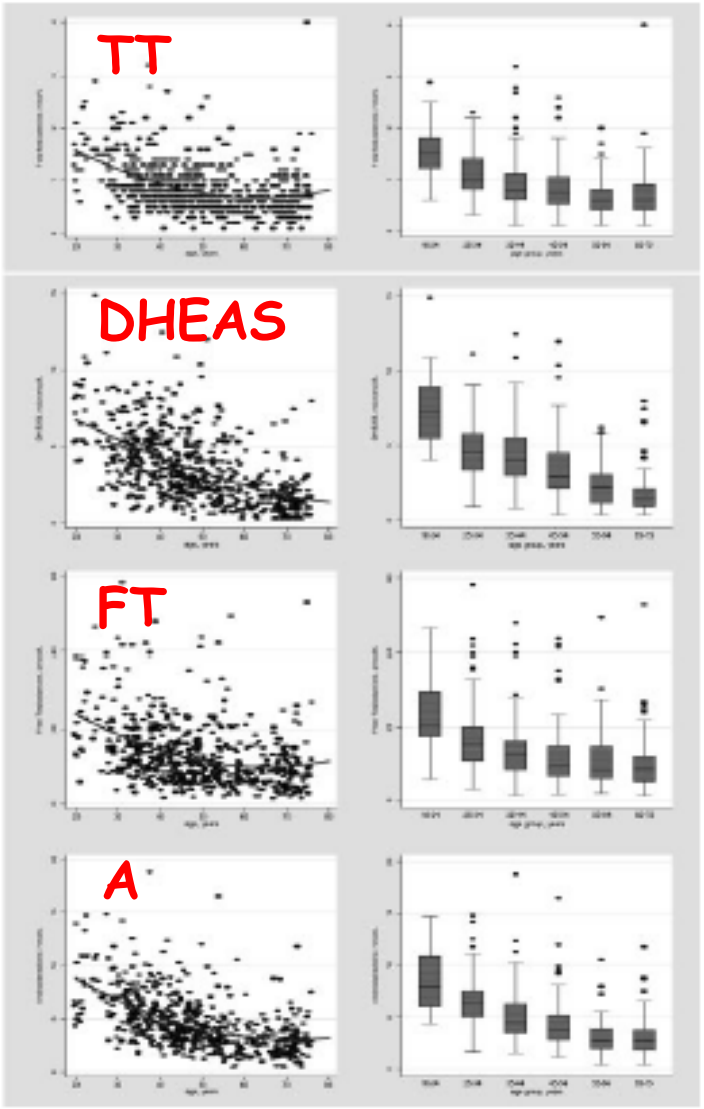
Lobo RA, 2001

ANDROGENS - EFFECT OF AGE & MENOPAUSE



Laughlin et al, 2000

ANDROGENS & AGING IN WOMEN



DIAGNOSIS of ANDROGEN INSUFFICIENCY is based on

- Symptoms (Type, Severity…)
- Circumstances (Premature Menopause…)
- ANDROGEN DECLINE IS RELATED TO AGE AND NOT TO NATURAL MENOPAUSE!!!
- DHEAS LEVELS SEEM ASSOCIATED TO WELL-BEING IN WOMEN AGED 45 YEARS OR OLDER

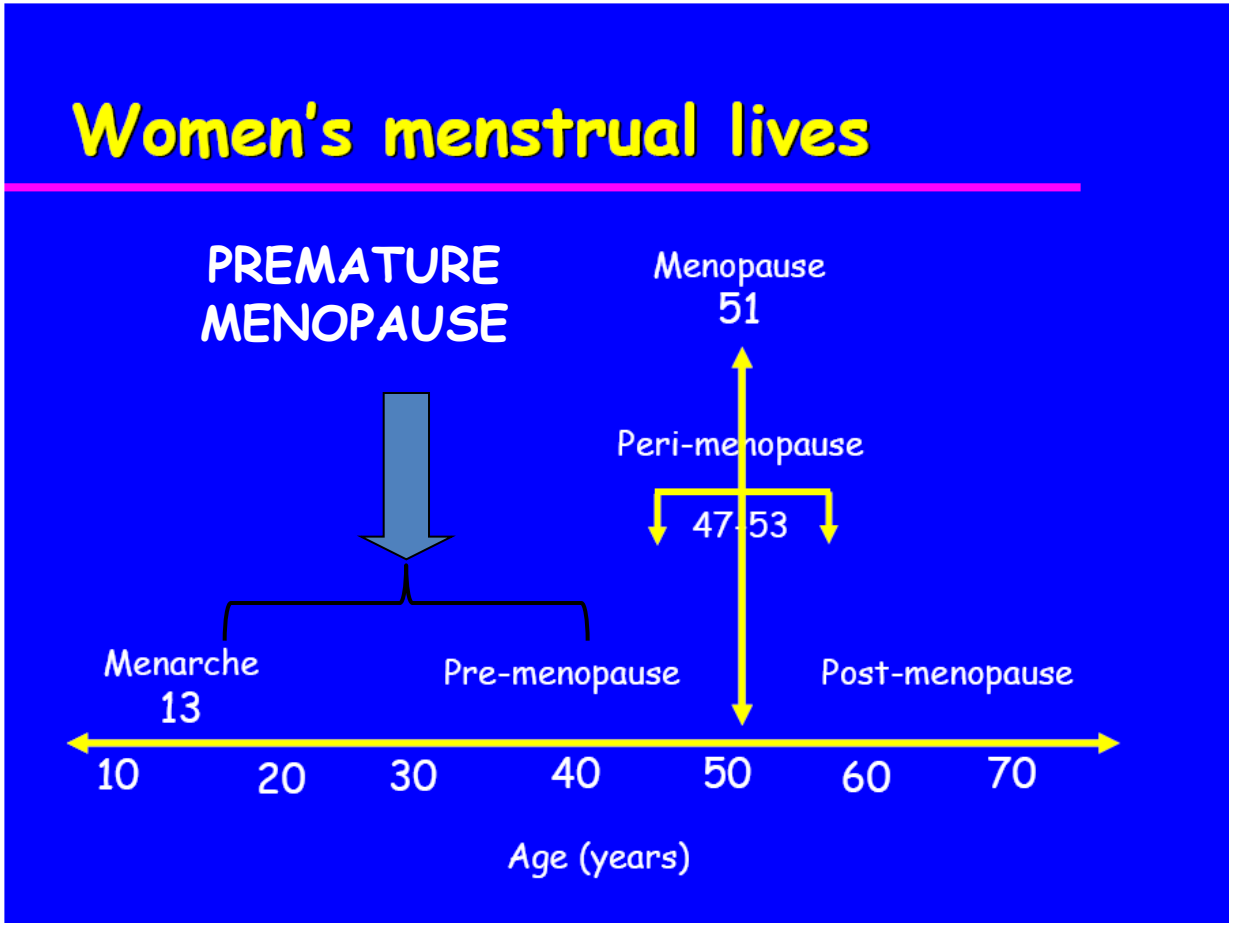
Simon, 2004;
Santoro et al, 2005;
Davis et al, 2005;
Davison et al, 2005

ANDROGENS & WOMEN'S HEALTH

- SEXUAL FUNCTION
- MOOD
- ENERGY
- COGNITION
- SENSE OF WELL-BEING
- BONE HEALTH
- MUSCLE MASS
- BODY COMPOSITION
- SKIN APPEARANCE
- *breasts, cardio-vascular function, reproduction, immune system…*

Cameron & Braunstein, 2004

AN EARLY EVENT IN THE AGING PROCESS



Population prevalence of 1% (varies by ethnicity) before the age of 40 yrs

Pol & Santoro, 2002; Luborsky et al, 2003

HEALTH CONSEQUENCES OF PREMATURE MENOPAUSE

- ✓ ENDOCRINE
- ✓ REPRODUCTIVE
- ✓ EMOTIONAL
- ✓ GENERAL

Mean life expectancy in women with menopause before the age of 40 years is 2.0 years shorter than in women with menopause after the age of 55 years.

★ *A SYSTEMIC DISORDER!*

LM Nelson, 2004; Ossewaarde et al, 2005

Primary ovarian insufficiency

Michel De Vos, Paul Devroey, Bart C J M Fauser

THE SAME IS TRUE FOR SURGICAL MENOPAUSE!!!

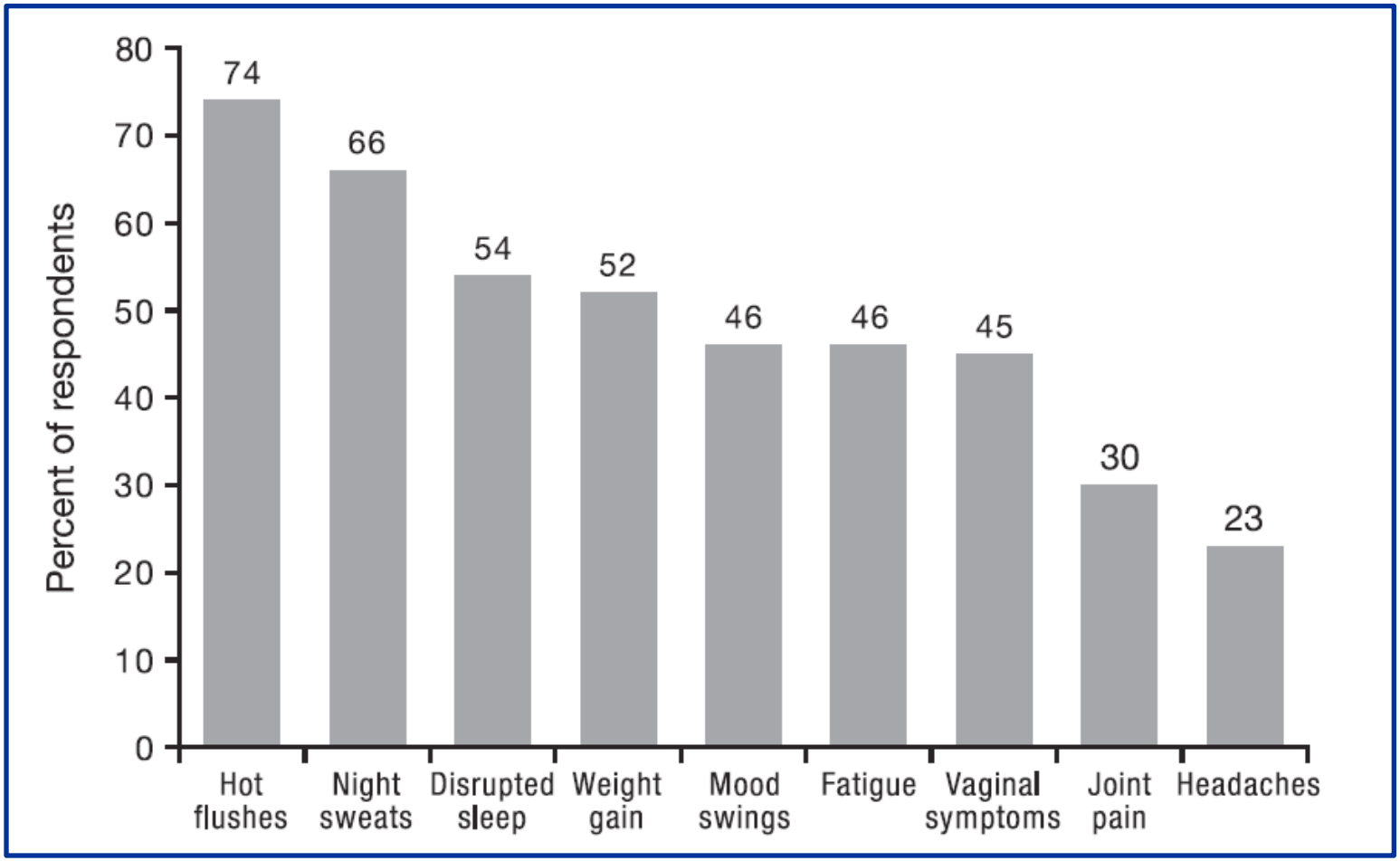
WOMEN'S HEALTH	EVIDENCE	REFERENCES
Infertility	strong	*Bidet, 2011*
Osteoporosis	strong	*Tolar, 2004; Rosen 2005; Sambrook, 2006*
Cognition/Alzheimer	strong	*Henderson 2007; Rocca 2007*
CVD/Mortality	strong	*Howard 2005; Rossouw 2007; Lobo 2007; Parker 2009*
Overall Mortality	strong	*Jacobsen, 2003; Rocca, 2006; Rivera 2009*
Parkinson	modest	*Rocca 2008*
Anxiety/Depression	modest	*Schmidt, 2006; Rocca 2008*

Lancet 2010; 376: 911–21

Vaginal Health: Insights, Views & Attitudes (VIVA) – results from an international survey

*R. E. Nappi and M. Kokot-Kierepa**

CLIMACTERIC 2012;15:36–44



- **3520 postmenopausal women aged 55–65 years**

INSTABILITA' NEUROENDOCRINA & EFFETTO "DOMINO"

modificato da CN Soares, 2010

Hot flashes are associated with increased ambulatory systolic blood pressure

Linda M. Gerber, PhD,[1,2] Lynnette Leidy Sievert, PhD,[3] Katherine Warren, BA,[1,2]
Thomas G. Pickering, MD, DPhil,[4] and Joseph E. Schwartz, PhD[2,5]

Menopause: The Journal of The North American Menopause Society
Vol. 14, No. 2, pp. 308-315

2007

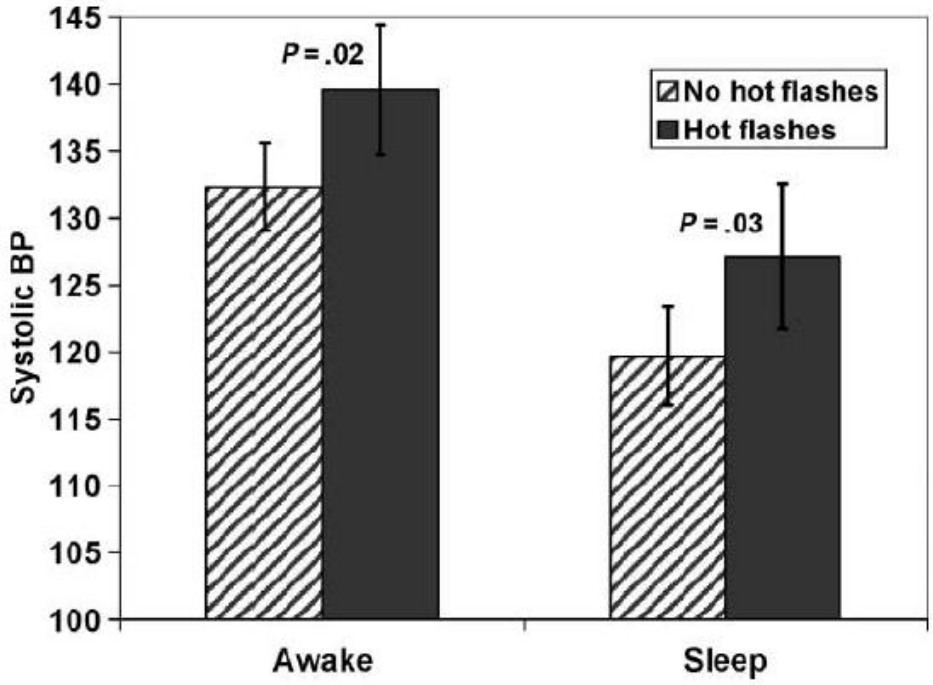
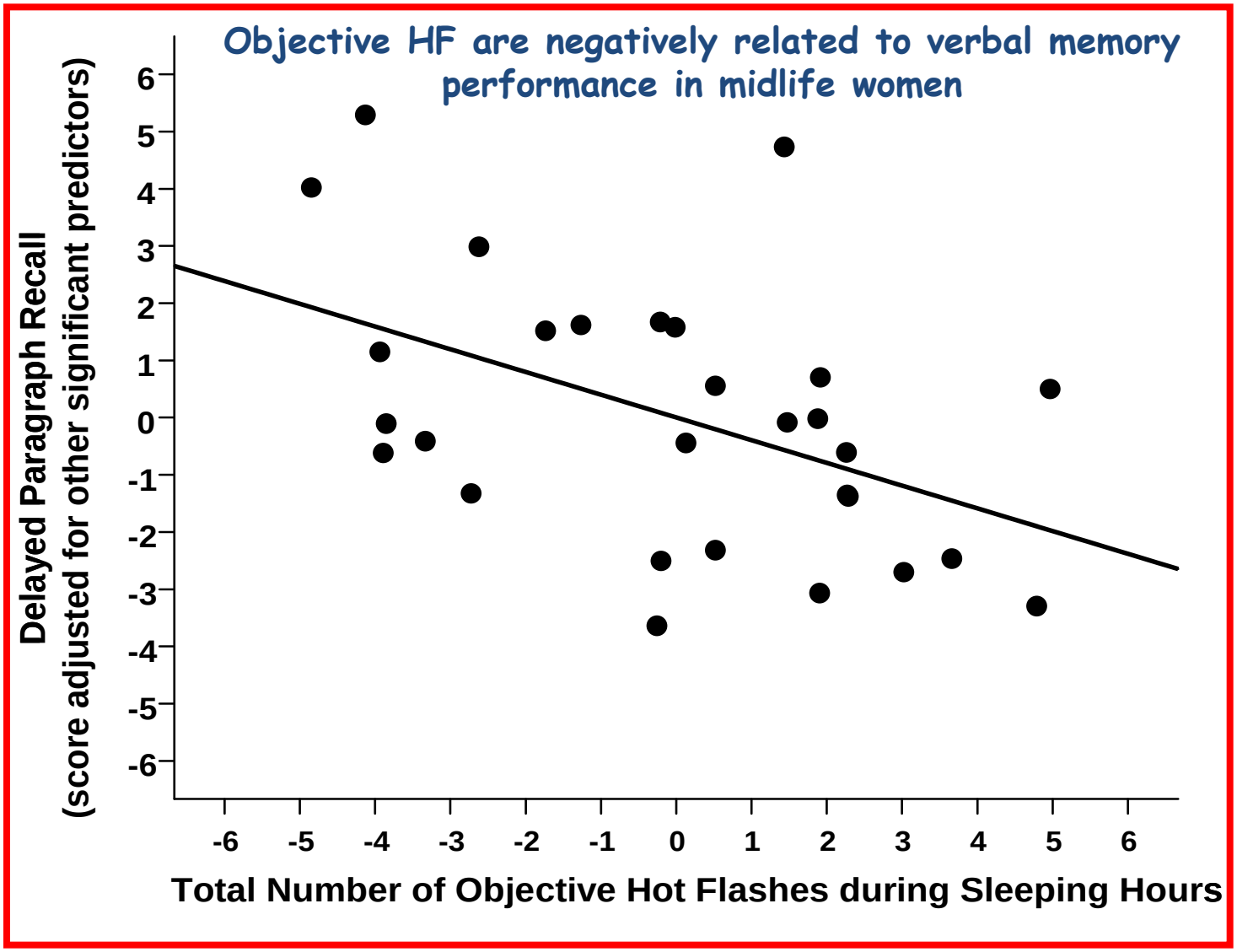


FIG. 3. Mean awake and sleep systolic blood pressures (BPs) by hot flash status adjusted for age, race/ethnicity, and body mass index.

HOT-FLUSHES AS A MARKER OF COGNITION



Maki et al, 2008

DEPRESSIVE SYMPTOMS THROUGHOUT THE MENOPAUSAL TRANSITION

- Longitudinal population-studies do not support an increase of depression at menopause, but they report a significant increase in mood lability during the perimenopausal period (up to 80%), followed by adaptation.

- Risk factors for the onset of menopausal depression (10%) are:
  - A history of "Reproductive" (premenstrual, postnatal) Depression;
  - Perimenopausal Period > 27 months;
  - Surgical Menopause;
  - Thyroid Dysfunctions.

Stewart et al, 1993; Avis et al, 1994

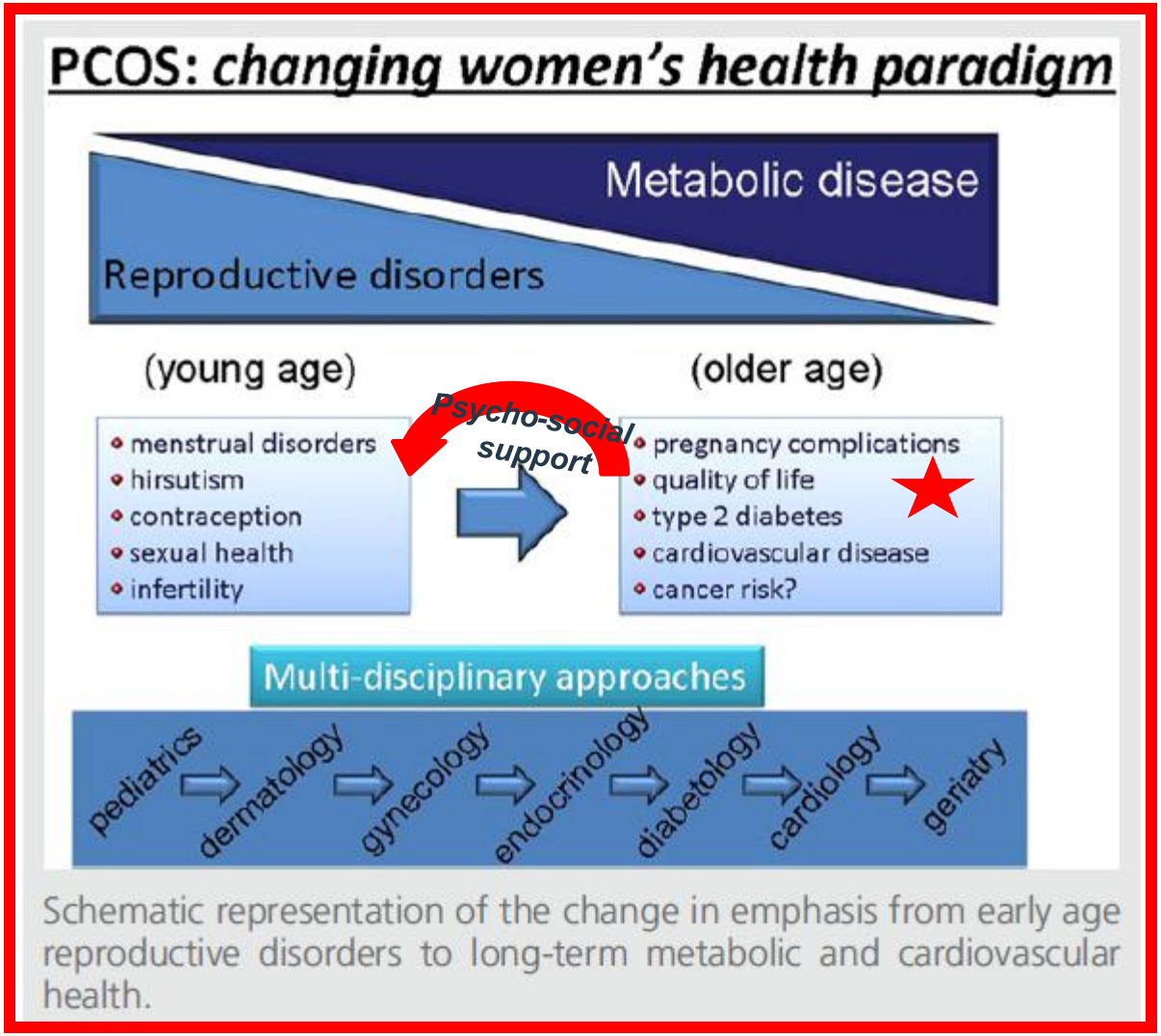
RELATIONSHIP BETWEEN DEPRESSION & MENOPAUSAL TRANSITION IS BIDIRECTIONAL

- Premenopausal women with a history of depression were 1.2 (0.9-1.6) times more likely to enter perimenopause early;
- Depressed women with more pronounced symptoms at study enrollment had twice the risk of an earlier perimenopausal transition;
- They were also 3 times more likely to have an early perimenopause if they were depressed and taking antidepressant medication at study entry;
- Women with a lifetime history of depression also had higher FSH and LH levels and lower E_2 levels at study enrollment and during the follow-up period after adjustment for covariates.

A lifetime history of major depression may be associated with an early decline in ovarian function

Harlow et al, 2003

Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ ASRM-Sponsored 3rd PCOS Consensus Workshop Group



Schematic representation of the change in emphasis from early age reproductive disorders to long-term metabolic and cardiovascular health.

modified from Fauser et al, 2012

CRITERI DIAGNOSTICI DELLA SINDROME METABOLICA

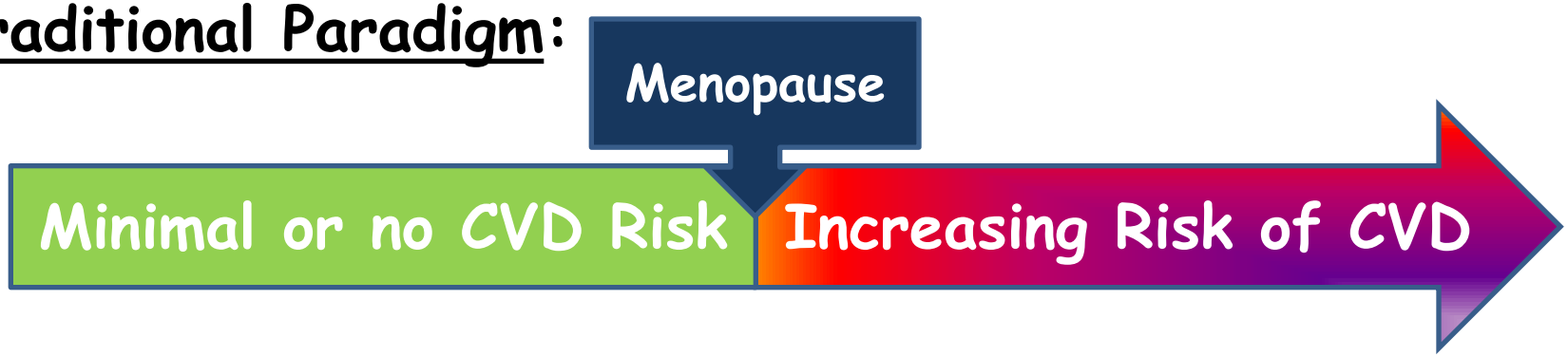
DONNA
Almeno 3 su 5

• CIRCONFERENZA VITA	> 88 CM
• TRIGLICERIDI	> 150 MG/DL
• HDL	< 50 MG/DL
• PRESSIONE ARTERIOSA	>/= 130/>/=85 MM HG
• GLICEMIA A DIGIUNO	>/= 110 MG/DL

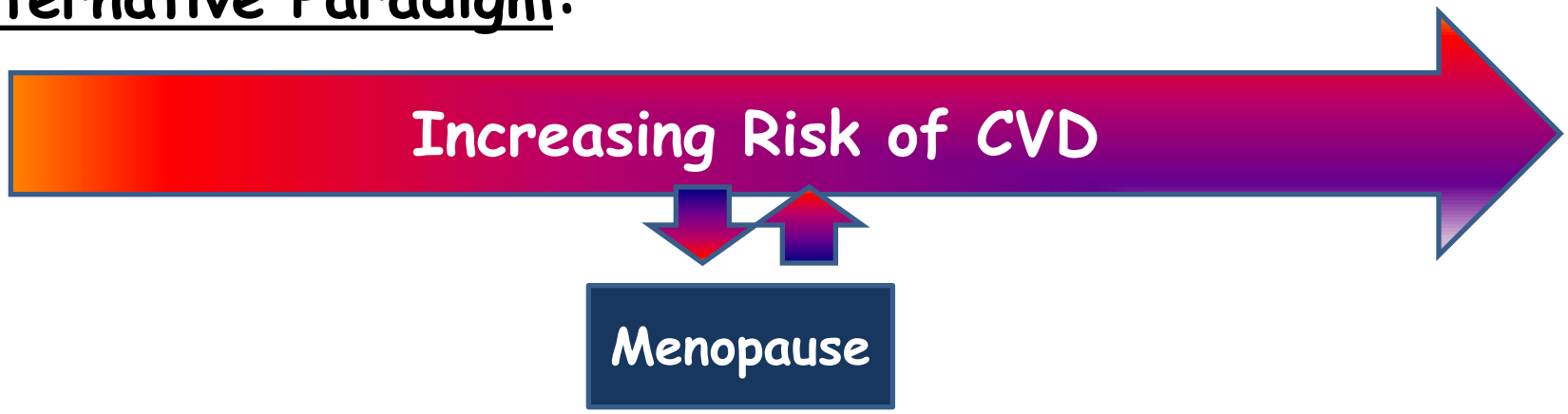
JAMA, 2001

CVD RISKS IN WOMEN IS ACROSS THE LIFE SPAN

Traditional Paradigm:

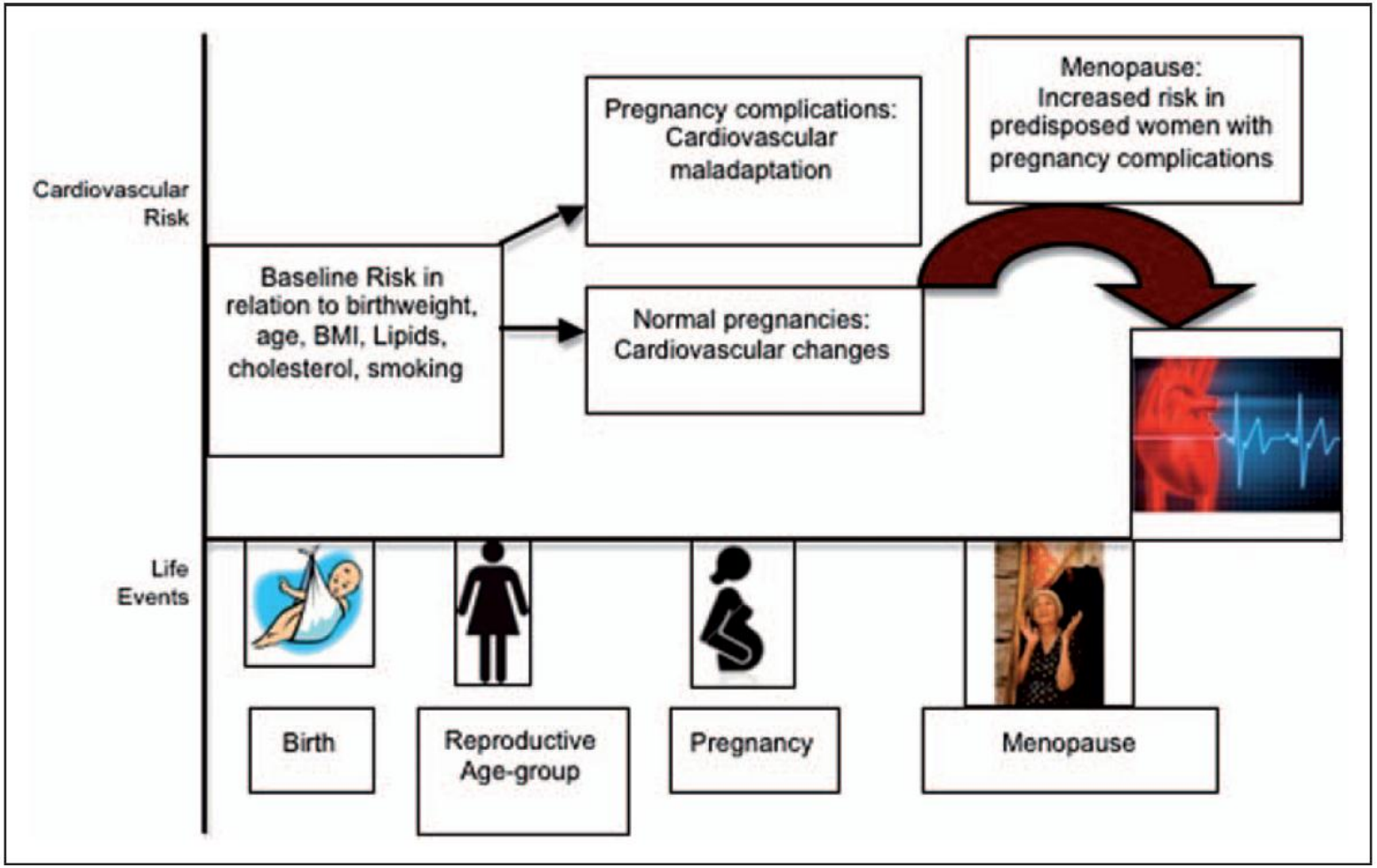


Alternative Paradigm:



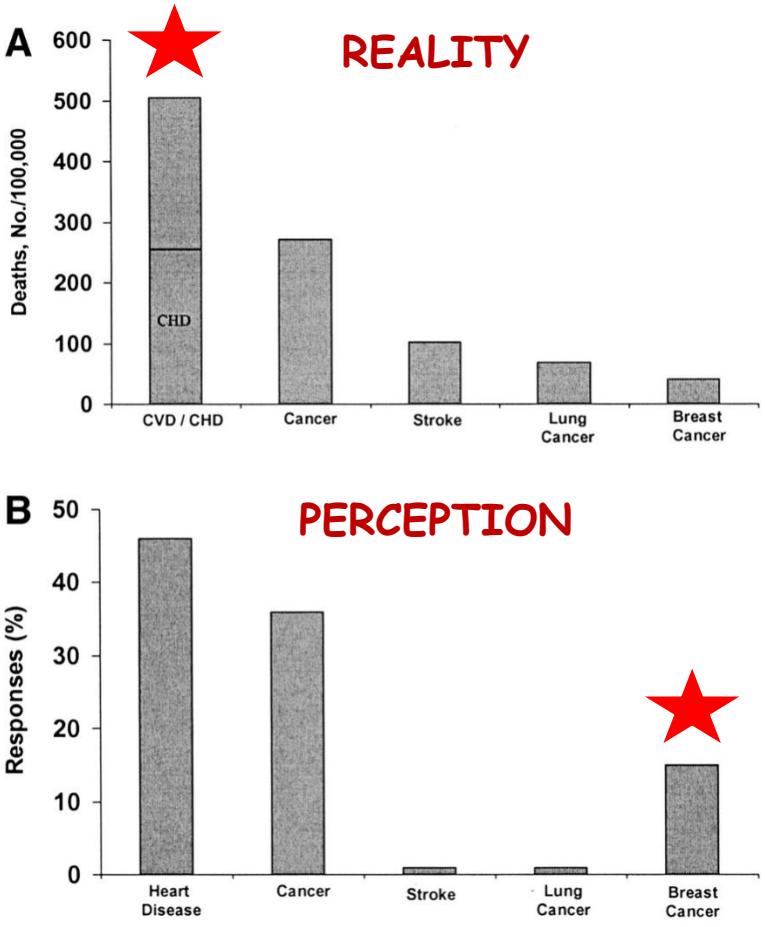
Adapted from Ehrenthal, 2010

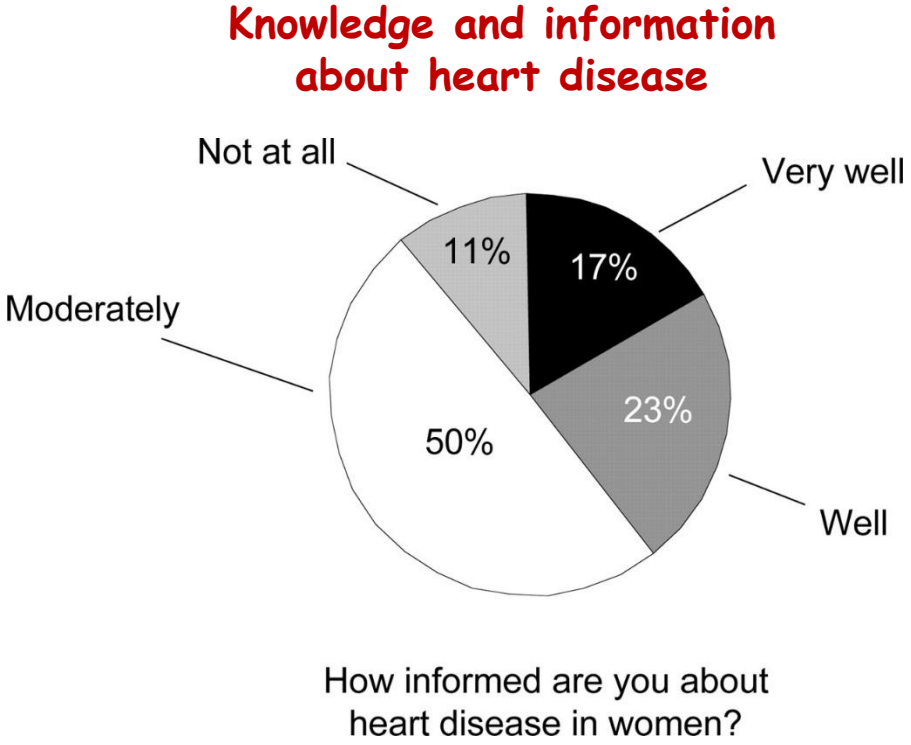
Cardiovascular disease in menopause: Does the obstetric history have any bearing?



Mahendru & Morris, 2013

WOMEN'S AWARENESS OF CVD RISK

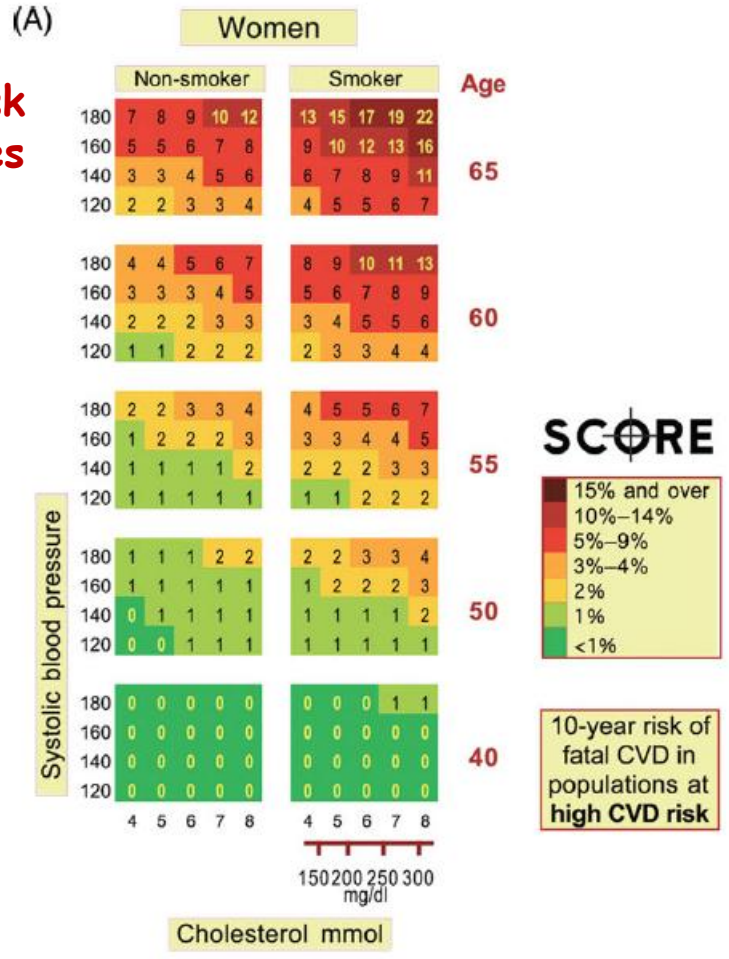




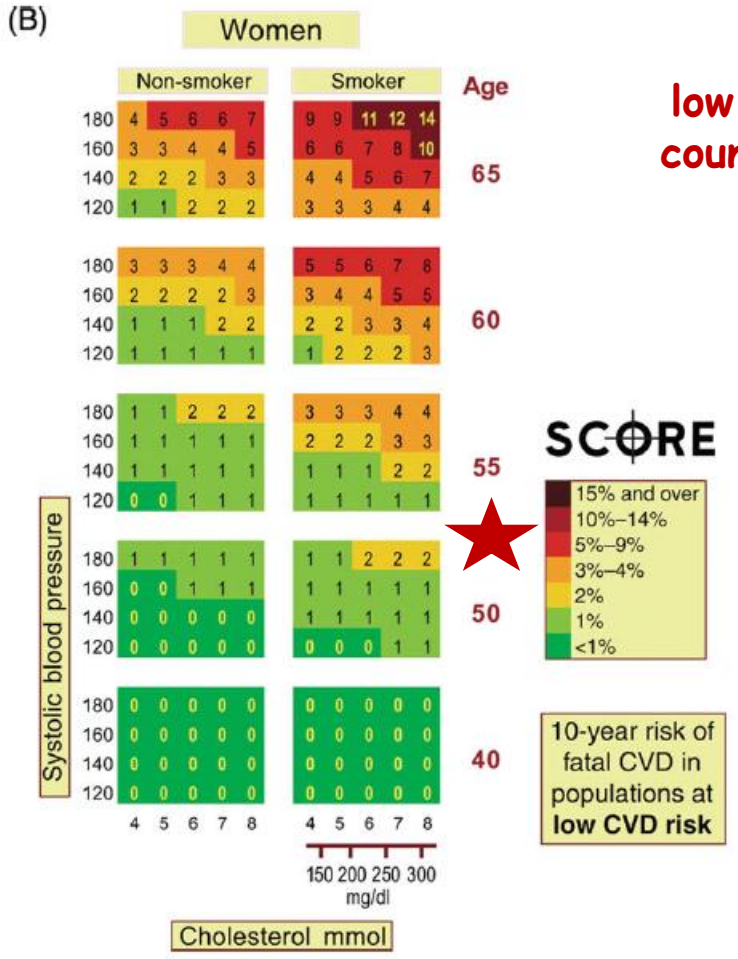
Mosca et al, 2004

European Society of Cardiology SCORE charts for women

high-risk countries



low-risk countries



Collins et al, 2007

BREAST CANCER ACROSS THE WORLD

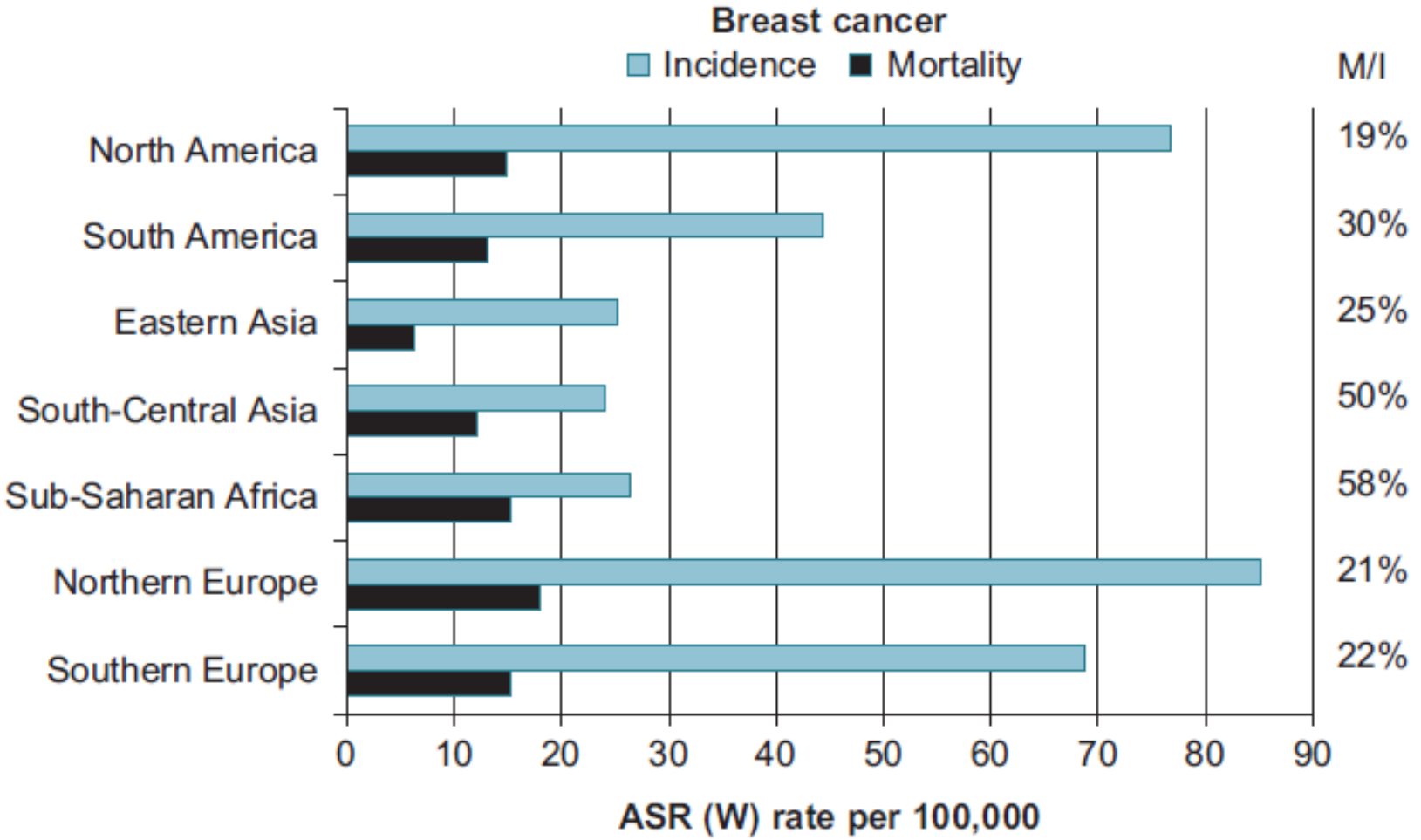


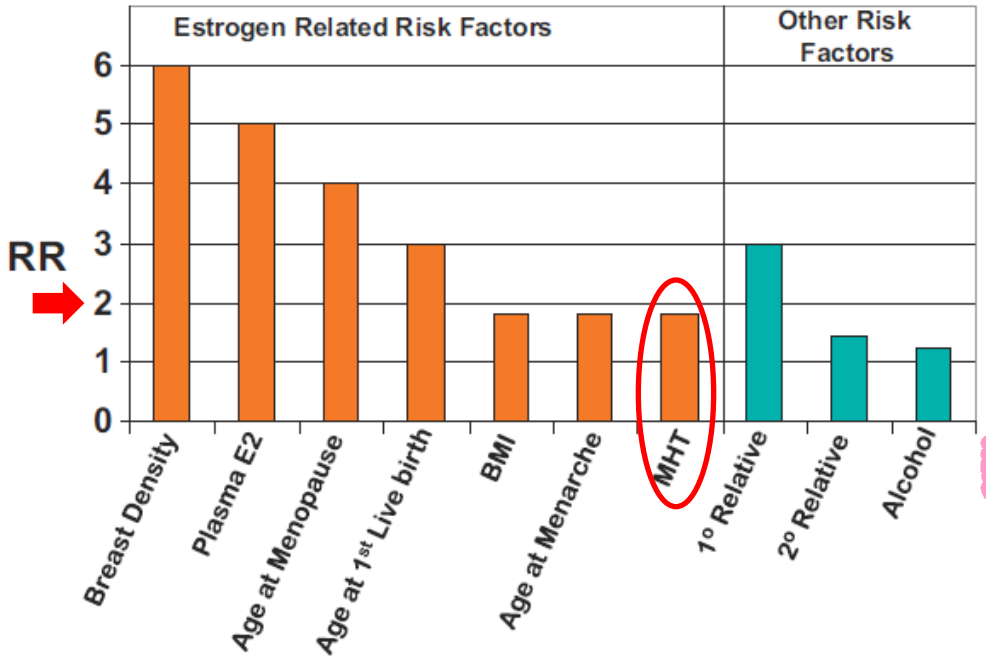
Figure 1 Breast cancer incidence and mortality rates as age-standardized rate adjusted to the world standard population (ASR (W)) per 100 000 women in seven main regions of the world (from Globocan 2008[5]). M/I, mortality to incidence ratio in percent

From Gompel et al, 2013

Menopausal hormone therapy and breast cancer

Richard J. Santen *

Journal of Steroid Biochemistry & Molecular Biology 142 (2014) 52–61



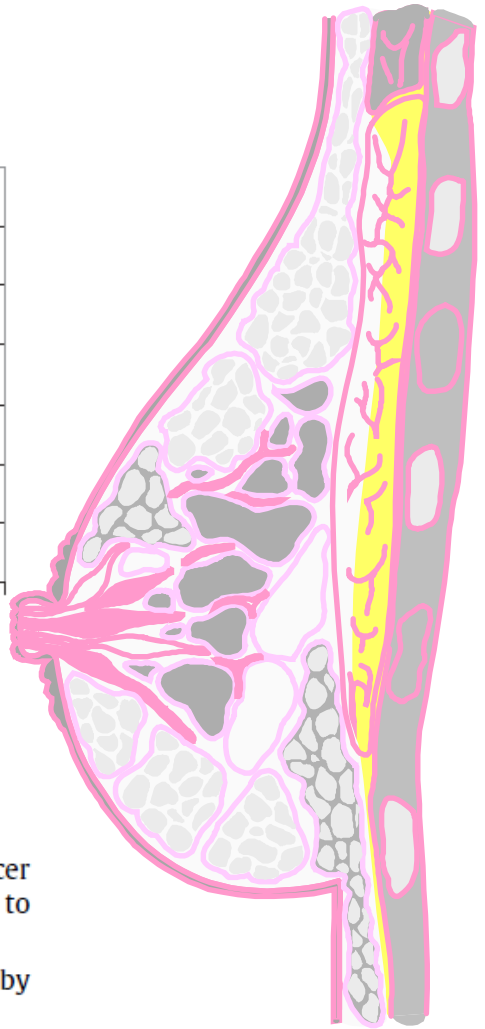


Fig. 1. Estrogen related risk factors for breast cancer. Risk factors for breast cancer related to clinical aspects that are associated with an increased chronic exposure to estradiol and expressed as relative risks (RR).

Figure adapted from the review of E. Amir et al. [83] and published in the article by Yager et al. [16]. Reproduced with the permission of the Endocrine Society.

The two strongest pieces of associative evidence implicating estrogen in women are that: (a) removal of both ovaries before the age of 35 reduces the lifetime risk of breast cancer by 75% and (b) women have a 100 fold higher risk of breast cancer than do men. This evidence is considered associative since the ovary also secretes progesterone and the differences between men and women could be related to a protective effect of testosterone. Additional epidemiologic data suggest that an increase in risk of breast cancer is associated with enhanced estrogen exposure during a woman's lifetime

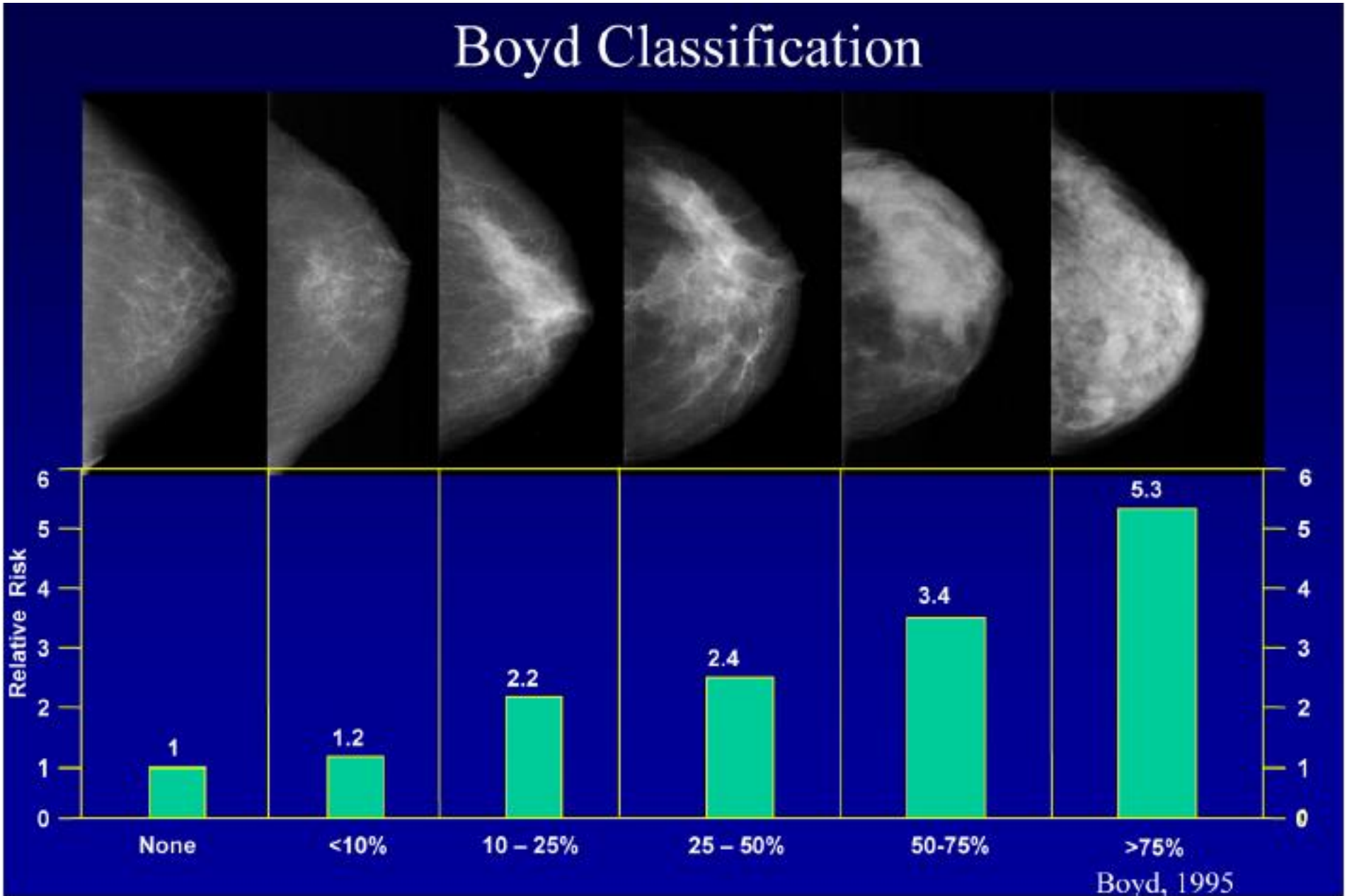
BREAST DENSITY & RISK

- 587 369 women had 1 349 027 mammographies
- 14090 breast cancers
- Birads 3 & 4 increased risk with HRT → to take into account

	BIRADS 1	BIRADS 2	BIRADS 3	BIRADS 4
Premenopausal	0.46 (0.37 - 0.58)	Reference	1.62 (1.51 - 1.75)	2.04 (1.84- 2.26)
Postmenopausal no HT	0.57 (0.53 -0.62)	Reference	**1.35 (1.28 - 1.42)**	**1.51 (1.35 - 1.68)**
Postmenopausal HT	0.50 (0.44 - 0.57)	Reference	**1.59 (1.51 - 1.69)**	**2.02 (1.83 - 2.22)**
Postmenopausal E	0.61 (0.48 - 0.78)	Reference	**1.60 (1.42 - 1.80)**	**1.99 (1.61 - 2.46)**
Postmenopausal E+P	0.45 (0.34 - 0.59)	Reference	**1.58 (1.44 - 1.74)**	**2.09 (1.79 - 2.43)**

Kerlikowske et al, 2010

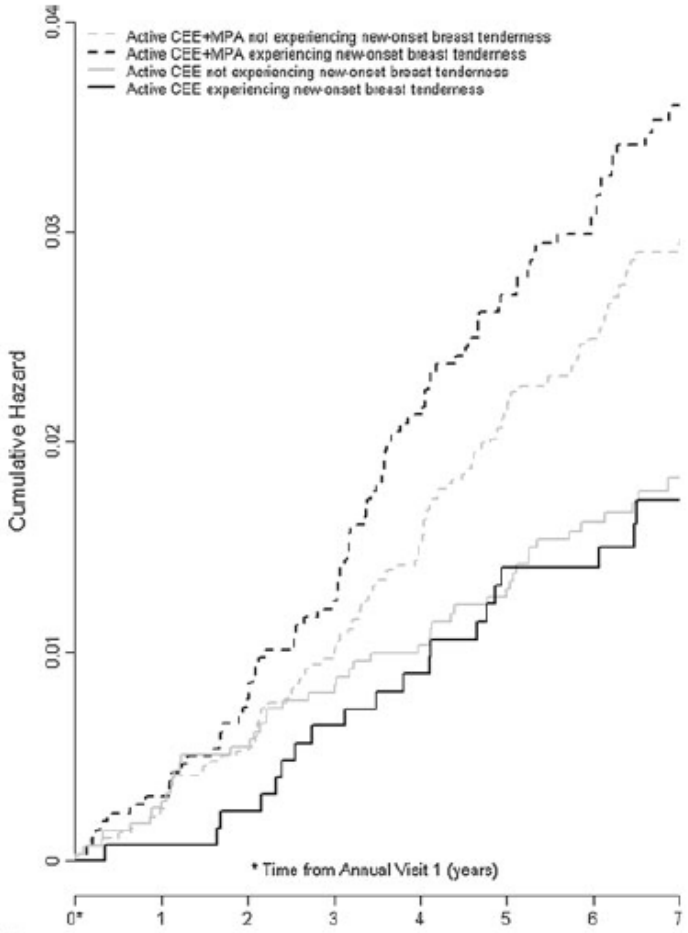
BREAST DENSITY & RISK



Mastalgia as a risk factor in WHI

If breast tenderness a baseline
HR: 2.16 (1.29 - 3.74)

If new onset BT
HR:1.33 (1.02 -1.72)



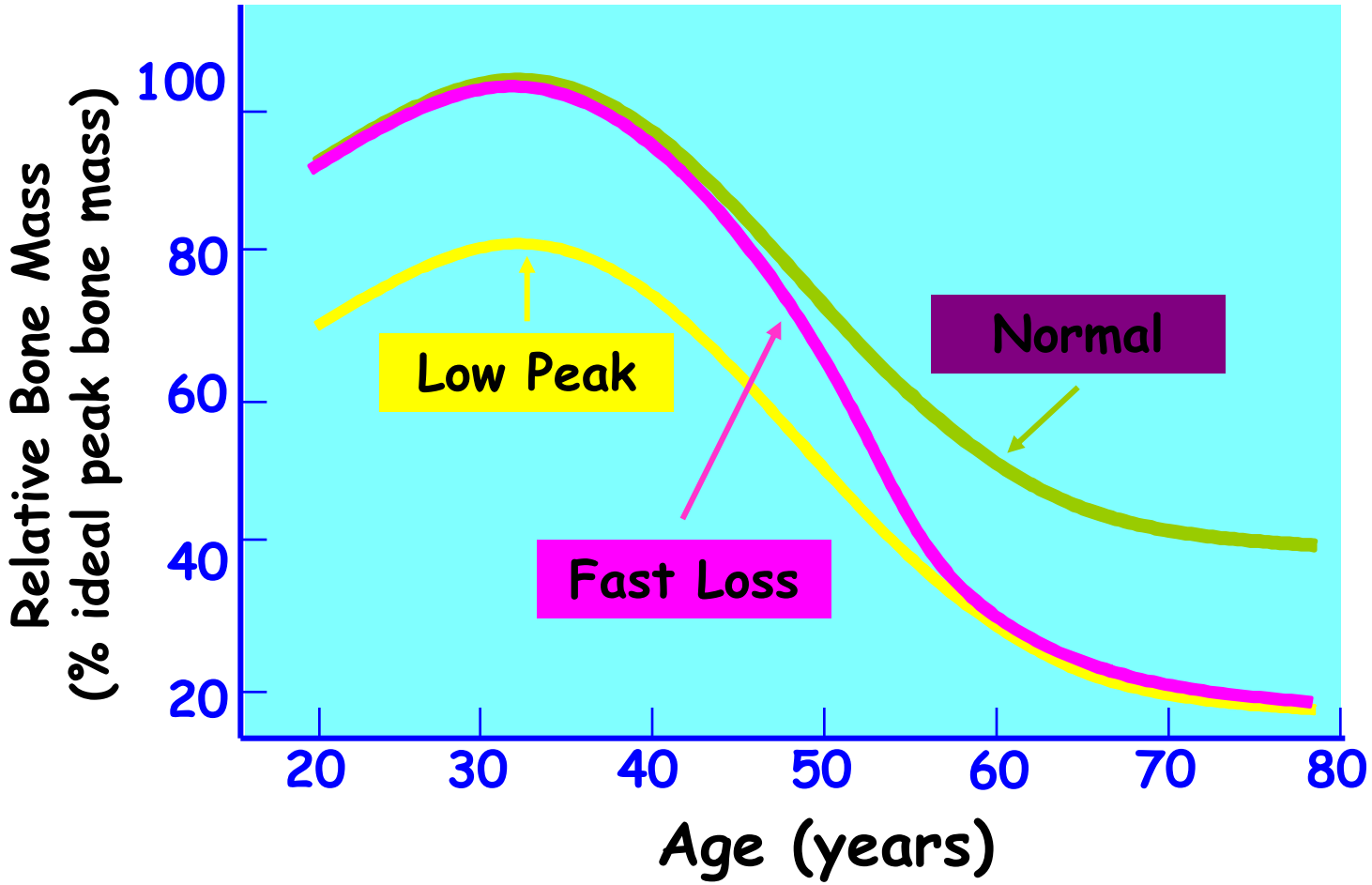
BT in EPT

No BT in EPT

BT
No BT in ET

Crandall et al, 2011

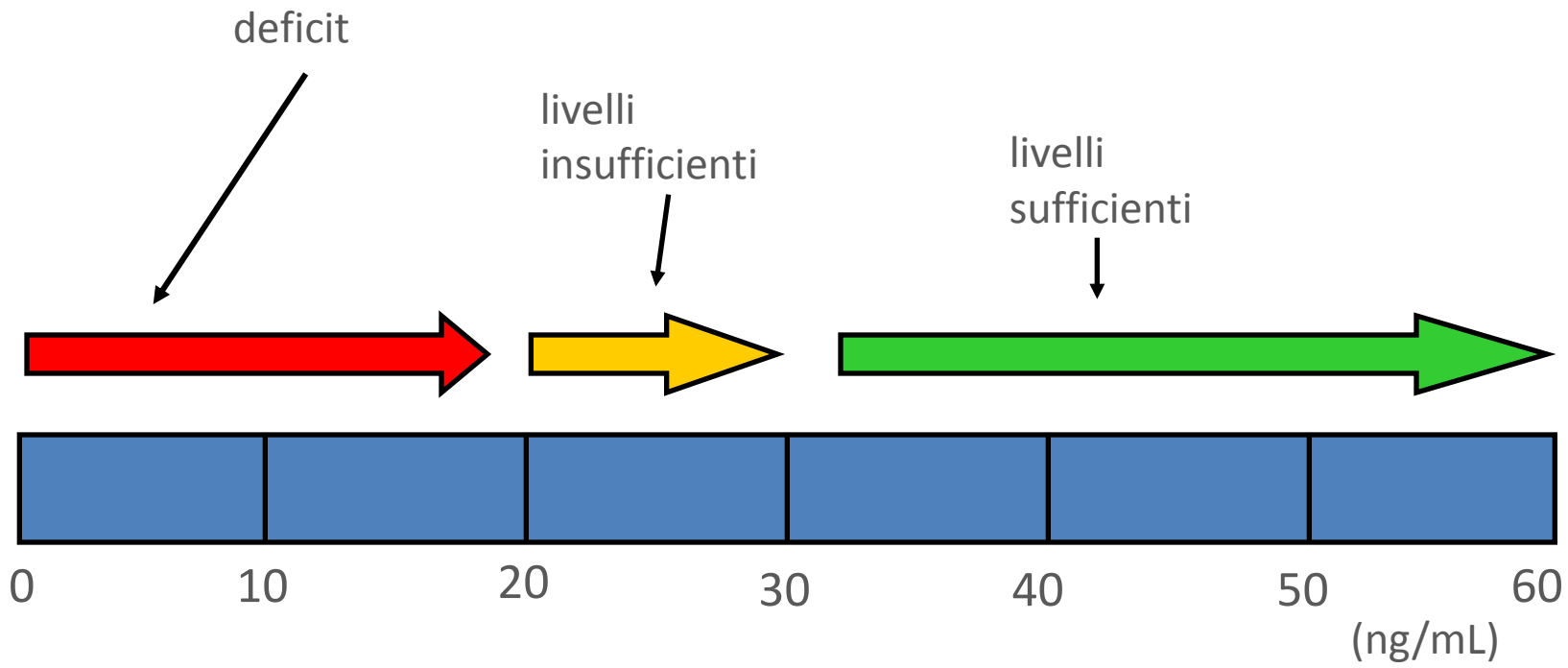
Bone Loss or Low Peak Bone Mass



ENDOGIN, 2015

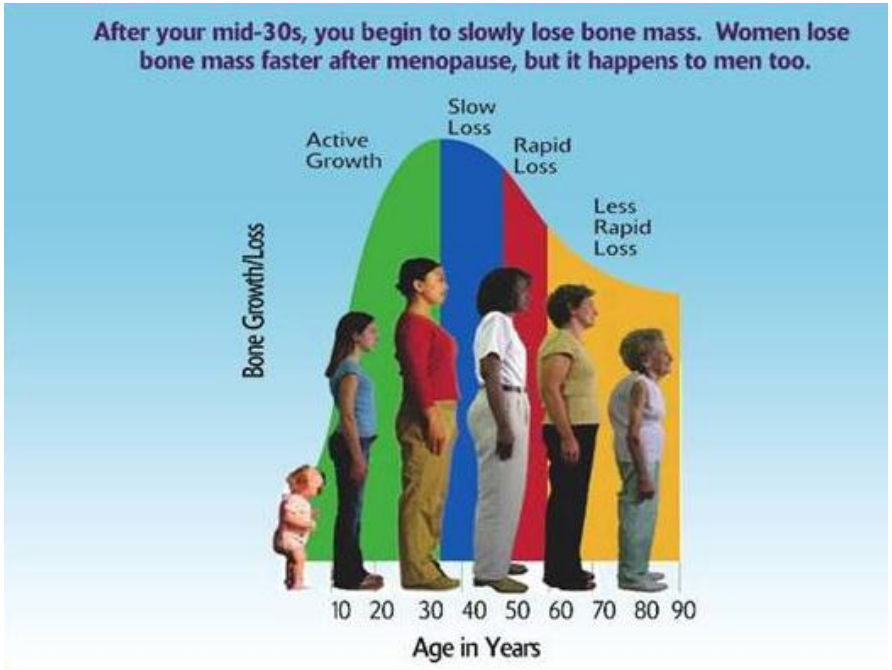
QUANTA VITAMINA D È NECESSARIA?

LIVELLI SIERICI DI VITAMINA D



Holick MF. N Engl J Med 2007;357:266-81.

BMD increases through young adulthood until achievement of peak BMD and then declines beginning in the fifth and sixth decades

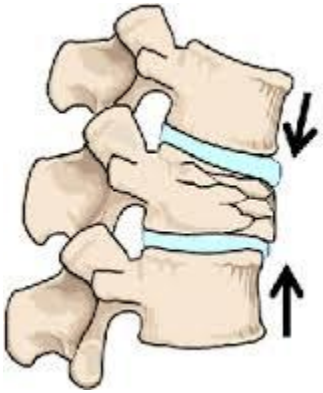


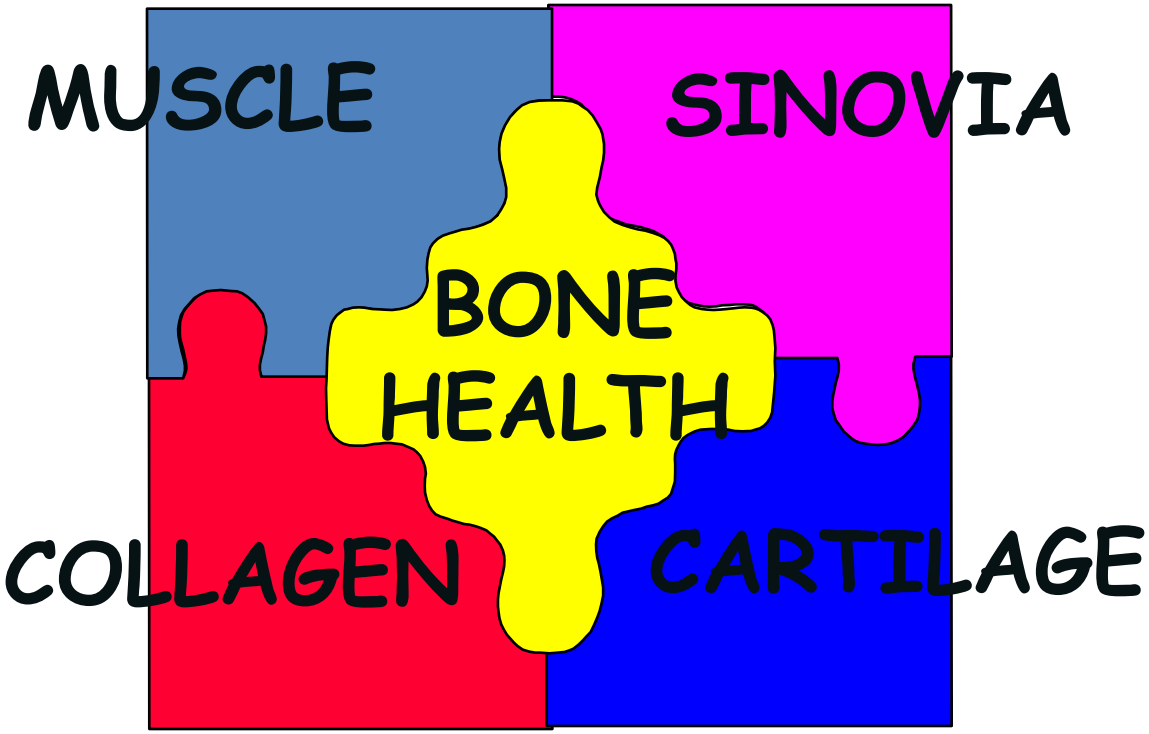
Variability in the rate of decline of BMD after young adulthood

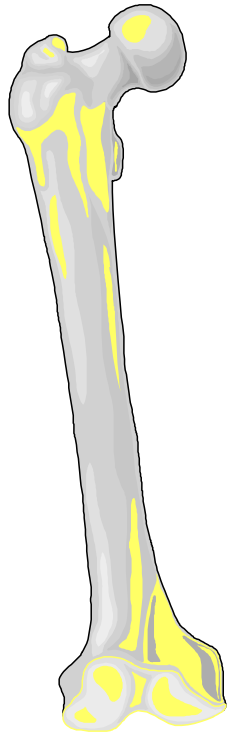
- ✓ **gender differences**
- ✓ **low body mass index**
- ✓ **Smoking**
- ✓ **weight loss**
- ✓ **loss of lean body mass and/or compromised nutritional status**
- ✓ **medications (*e.g. glucocorticoids, androgen* deprivation therapy, and aromatase inhibitors)**

Ensrud et al, 1995 J Bone Miner Res ; Greenspan et al, 1994 J Bone Miner Res ; Jones et al, 1994 BMJ ; Smith et al, 1999 J ClinDensitom ; Burger et al, 1998 Am J Epidemiol ; Hannan et al, 2000 J Bone Miner Res ; Nguyen et al, 1998 J Bone Miner Res ; Dennison et al, 1999 Osteoporos ; Weng et al, 2007 Curr Osteoporos Rep

SEX STEROIDS & MUSCOLO-SKELETAL SYSTEM







ENDOGIN, 2014

EPIDEMIOLOGY OF RHEUMATIC ADs & REPRODUTIVE LIFE SPAN

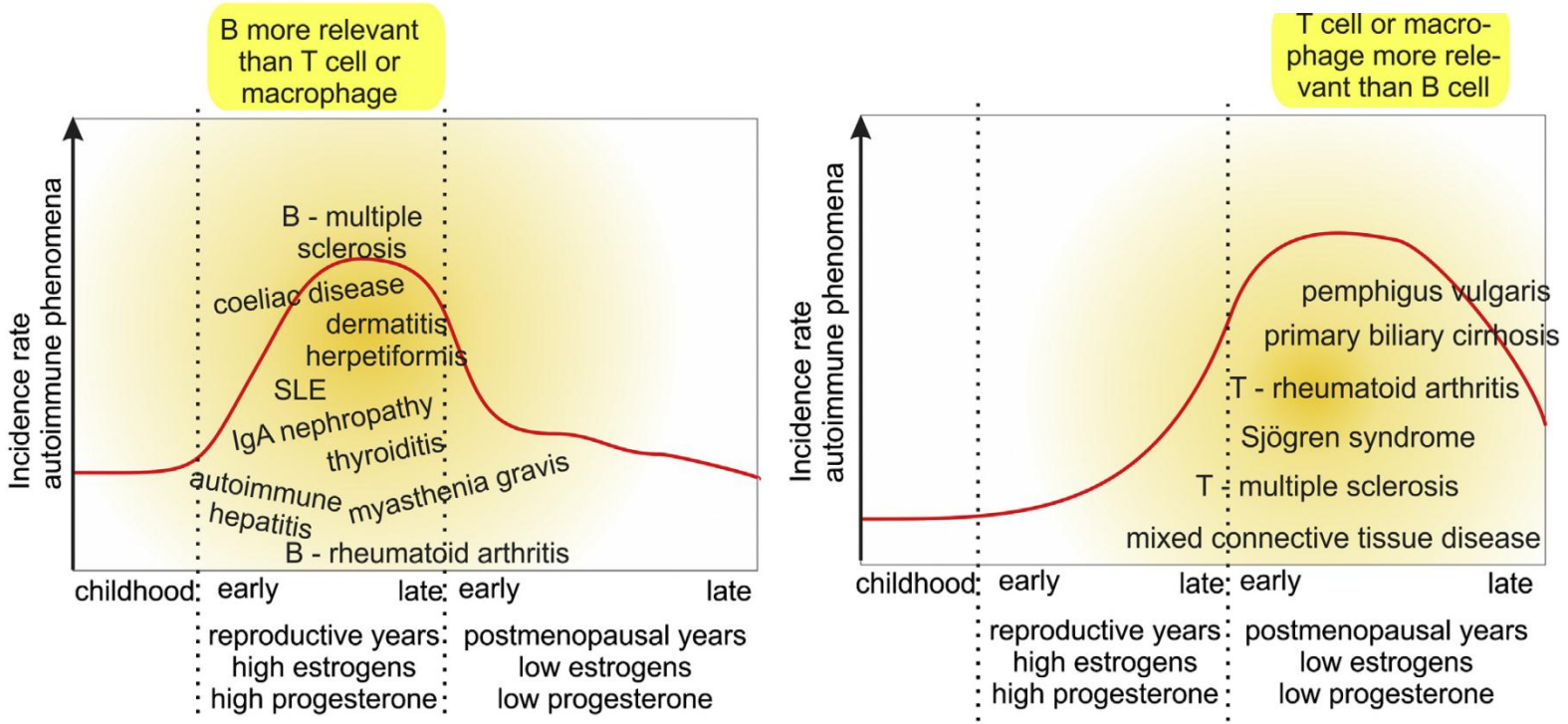
Table 1

Sex ratios for connective tissue autoimmune diseases

Oliver & Silman, 2009

Disease	Female:male ratio	Peak age at onset	Reference
Rheumatoid arthritis	2:1 to 3:1	Forties	[83]
Systemic lupus erythematosus	9:1	Late teens to early forties	[6]
Systemic sclerosis	3:1	Forties[a]	[4]

[a]Known to vary due to ethnicity.



Straub et al, 2013

THYROID & MENOPAUSE

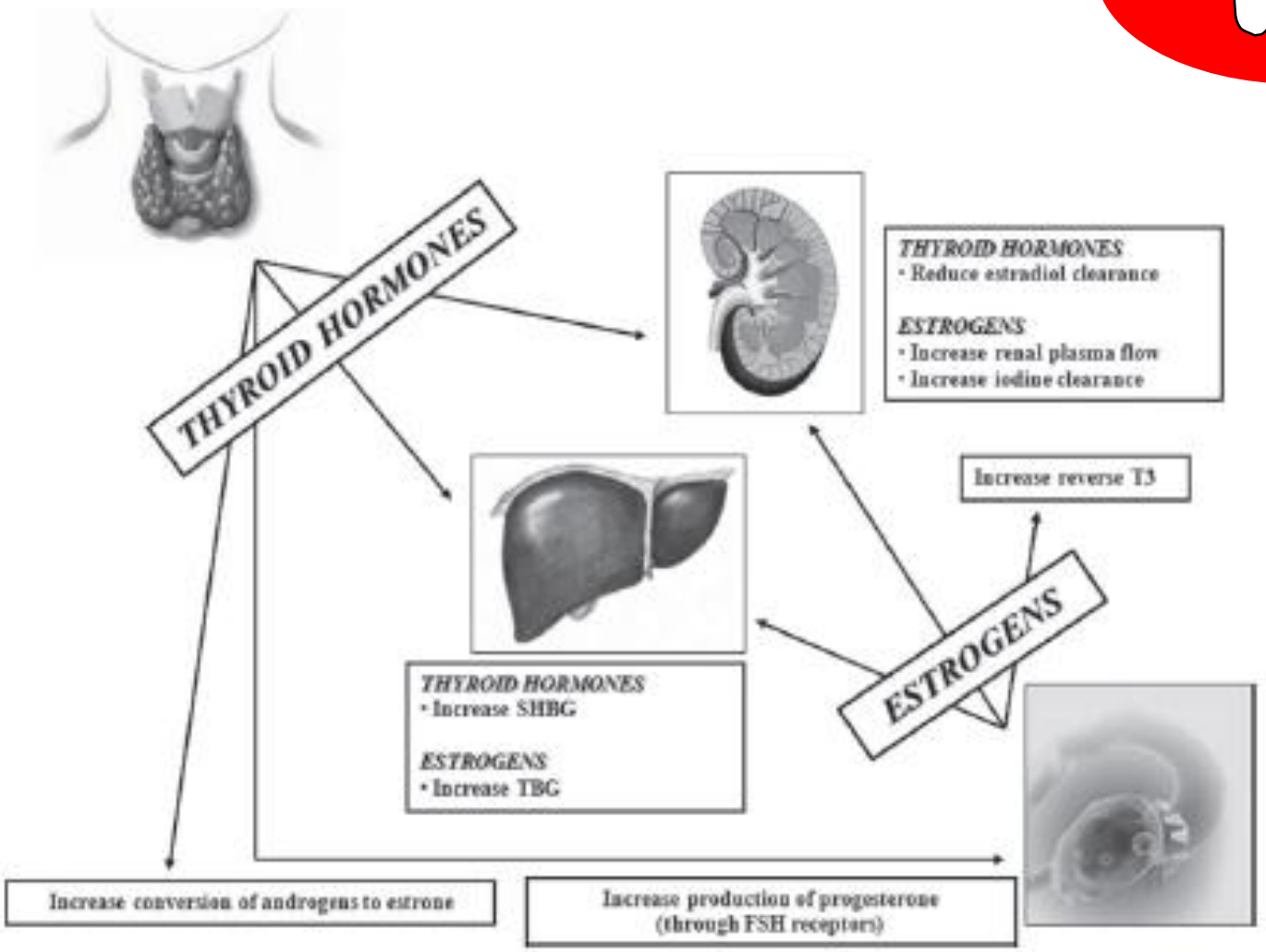


Figure 1 Schematic diagram explaining the relationship between thyroid, ovary, liver and kidney; actions of thyroid hormones, estrogens. T3, triiodothyronine; SHBG, sex hormone binding globulin; TBG, thyroxine binding globulin; FSH, follicle stimulating hormone

Del Ghianda et al, 2014

THYROID & MENOPAUSE

Table 3 Signs and symptoms common to both hypothyroidism/hyperthyroidism and menopause

Hypothyroidism 10-20%	*Hyperthyroidism* 2-4%
Skin atrophy	Hot flushes
Constipation	Heat intolerance and sweating
Brittle hair	Palpitations
Periorbital edema	Irritability
Weight gain	Insomnia
Constipation	

Del Ghianda et al, 2014

DRUGS ASSOCIATED WITH SEXUAL DYSFUNCTION

Drug class	Decreased desire	Decreased arousal	Orgasm or ejaculatory difficulties
Antidepressants	amitriptyline clomipramine fluoxetine imipramine paroxetine phenelzine sertraline	amitriptyline citalopram clomipramine doxepin fluoxetine imipramine nortriptyline paroxetine phenelzine sertraline tranylcypromine	citalopram clomipramine doxepin escitalopram fluoxetine* fluvoxamine imipramine nortriptyline paroxetine* sertraline* tranylcypromine venlafaxine
Other psychotropic drugs	alprazolam chlorpromazine fluphenazine haloperidol lithium risperidone	chlorpromazine fluphenazine lithium risperidone	alprazolam fluphenazine haloperidol risperidone
Cardiovascular drugs	clonidine digoxin hydrochlorothiazide methyldopa spironolactone	beta blockers clonidine digoxin hydrochlorothiazide methyldopa perhexilene spironolactone	
Other drugs	cimetidine	antihistamines cimetidine cyproterone disulfiram gonadotrophin-releasing hormone agonists propantheline pseudoephedrine	naproxen

* common cause of orgasmic difficulty

Conagan & Conagan, 2013

ELEMENTI CRITICI NEL CICLO VITALE DELLA DONNA

- **PERCEZIONE DI SE'**
  (Femminilità, Estetica)
- **PROGETTO DI VITA**
  (Coppia, Ruolo Sociale)
- **ASPETTATIVE DI SALUTE**
  (Età Biologica vs Età Anagrafica)

RE Nappi, 2006

PUNTI BASE DELLA FENOTIPIZZAZIONE DELLA DONNA IN MENOPAUSA

- ETA' DELLA MENOPAUSA
- STORIA FAMILIARE
- STORIA DEI CICLI MESTRUALI
- PESO
- PRESSIONE ARTERIOSA
- COMORBIDITA'
- FARMACI
- PARITA'
- STORIA OSTETRICA
- USO PREGRESSO DI ORMONI

- COPPIA STABILE
- ATTIVITA' LAVORATIVA
- ATTITUDINI

MENOPAUSAL SYMPTOMS & CLINICAL RESPONSES TO HORMONE THERAPY ARE UNIQUE TO EACH INDIVIDUAL WOMAN

- Estrogen receptor
  - Type
  - Distribution
  - Activity
- Estrogen synthesis and metabolism
  - CYP 450 genotype
  - Sulfatase activity
  - Aromatase activity
  - 17β-OH dehydrogenase activity
  - COMT activity
- Bioavailable estrogen/androgen
  - SHBG
  - "Hormone threshold"

Courtesy of M Notelovitz, 2003

PHARMACOGENETICS & PHARMACOGENOMICS (PGx)

- PHARMACOGENETICS: the study of inter-individual specific genetic variation related to drug response (both safety and efficacy)

- PHARMACOGENOMICS: the study of genomics and proteomics information for identifying new drug targets and their mechanisms of action

The goal is to improve therapy on the basis of genetic information for each individual patient taking gender into account.

ESTO, 2006

INDIVIDUALIZING HT WITH PGx – VANITY OR VANGUARD?

- The endocrinology of the menopausal transition is complex.
- Advances in molecular and genomic science have confirmed that every woman is unique and has a *thumbprint* that will determine her response to physiologic events and to lifetime risks of disease.
- Variations in the genetically determined biology of women will determine the symptomatic response of a given menopausal woman to her physiologic decrease in estrogen synthesis and postmenopausal metabolism to her response (or non response) to HT.

M Notelovitz, 2007

Hormone Therapy and the Risk of Breast Cancer in *BRCA1* Mutation Carriers

Andrea Eisen, Jan Lubinski, Jacek Gronwald, Pal Moller, Henry T. Lynch, Jan Klijn, Charmaine Kim-Sing, Susan L. Neuhausen, Lucy Gilbert, Parviz Ghadirian, Siranoush Manoukian, Gad Rennert, Eitan Friedman, Claudine Isaacs, Eliot Rosen, Barry Rosen, Mary Daly, Ping Sun, Steven A. Narod, and the Hereditary Breast Cancer Clinical Study Group

Background Hormone therapy (HT) is commonly given to women to alleviate the climacteric symptoms associated with menopause. There is concern that this treatment may increase the risk of breast cancer. The potential association of HT and breast cancer risk is of particular interest to women who carry a mutation in *BRCA1* because they face a high lifetime risk of breast cancer and because many of these women take HT after undergoing prophylactic surgical oophorectomy at a young age.

Methods We conducted a matched case–control study of 472 postmenopausal women with a *BRCA1* mutation to examine whether or not the use of HT is associated with subsequent risk of breast cancer. Breast cancer case patients and control subjects were matched with respect to age, age at menopause, and type of menopause (surgical or natural). Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated with conditional logistic regression. Statistical tests were two-sided.

Results In this group of *BRCA1* mutation carriers, the adjusted OR for breast cancer associated with ever use of HT compared with never use was 0.58 (95% CI = 0.35 to 0.96; $P = .03$). In analyses by type of HT, an inverse association with breast cancer risk was observed with use of estrogen only (OR = 0.51, 95% CI = 0.27 to 0.98; $P = .04$); the association with use of estrogen plus progesterone was not statistically significant (OR = 0.66, 95% CI = 0.34 to 1.27; $P = .21$).

Conclusion Among postmenopausal women with a *BRCA1* mutation, HT use was not associated with increased risk of breast cancer; indeed, in this population, it was associated with a decreased risk.

J Natl Cancer Inst 2008;100:1361–1367

ESTROGEN-RECEPTOR POLYMORPHISMS & HDL CHOLESTEROL

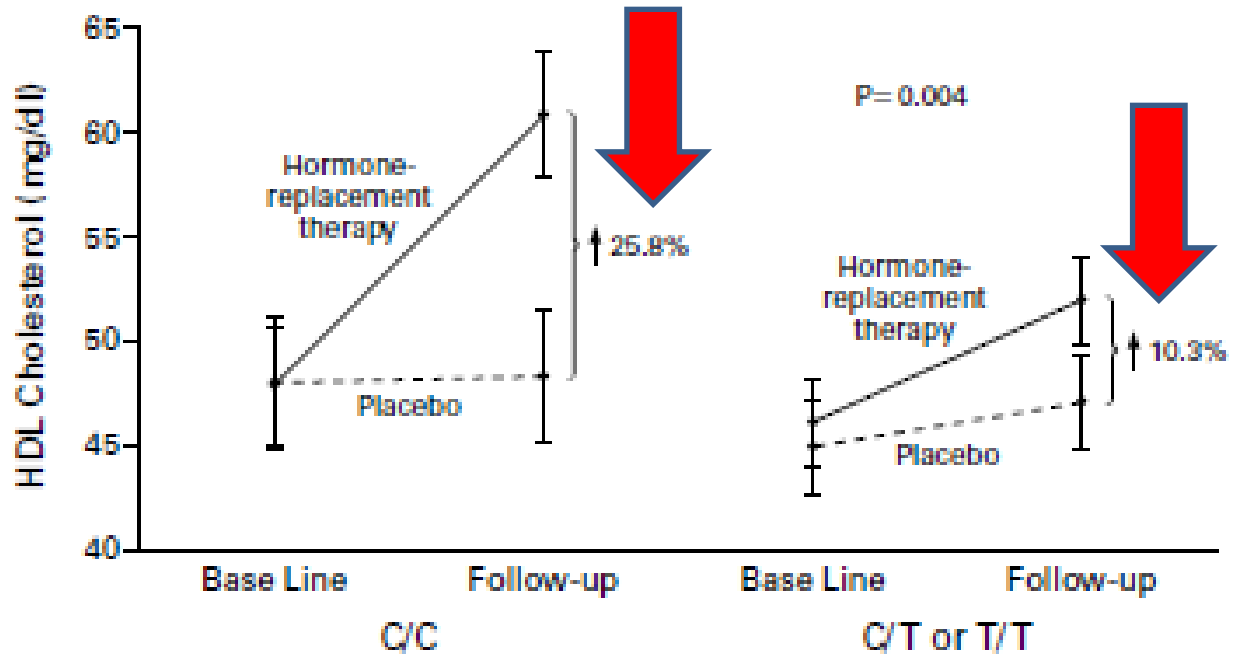
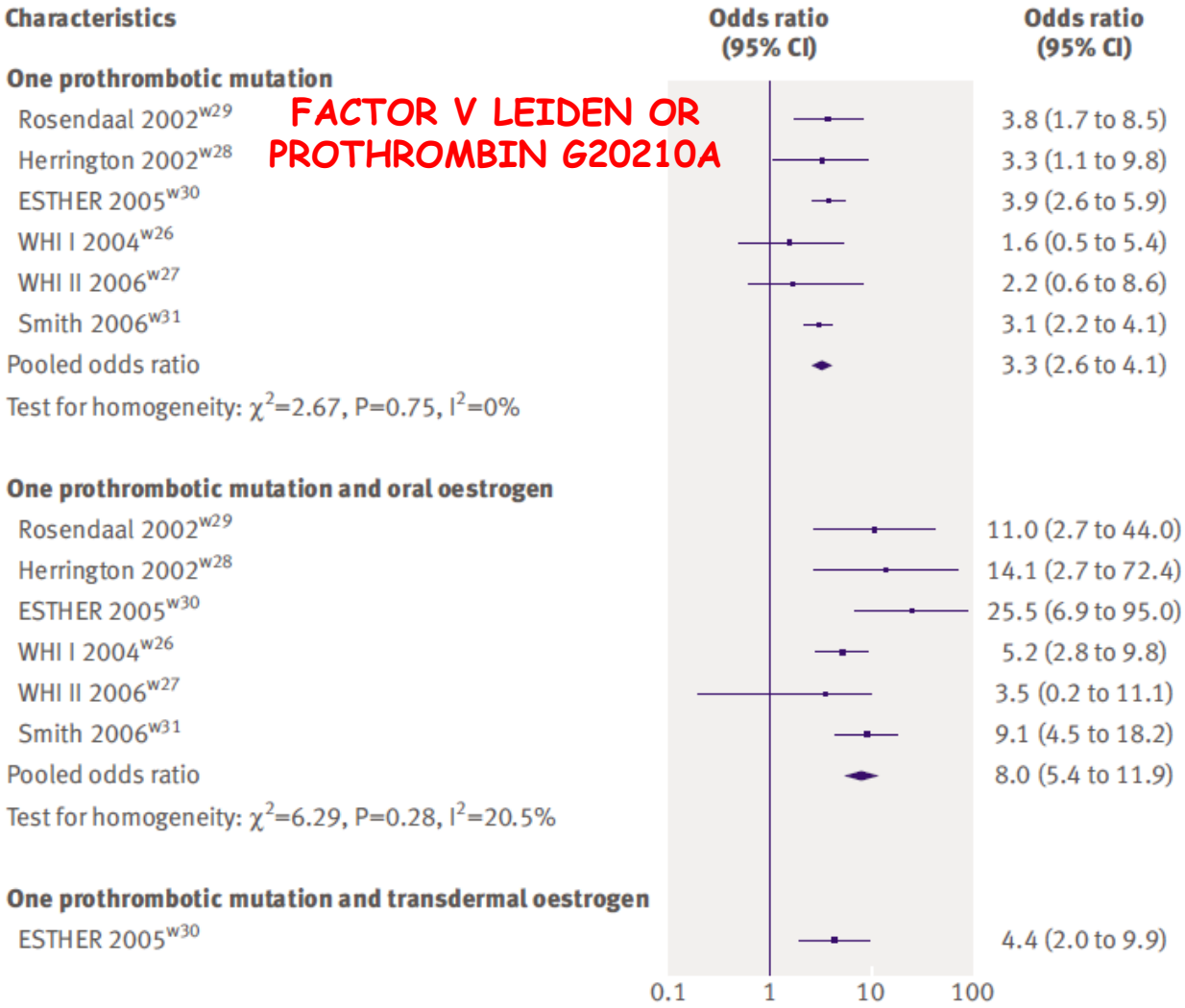


Figure 2. Mean (±SE) High-Density Lipoprotein (HDL) Cholesterol Levels at Base Line and Follow-up among Women in the Estrogen Replacement and Atherosclerosis Trial According to Study Group and Human Estrogen Receptor α IVS1−401 Genotype, with Adjustment for Age, Race or Ethnic Group, Body-Mass Index, Diabetes Status, Smoking Status, Frequency of Exercise, and Alcohol Intake.
The P value is for the treatment-by-genotype interaction. To convert values for cholesterol to millimoles per liter, multiply by 0.02586.

Herrington et al, 2002

RISKS OF VTE BY ROUTE OF HRT AND PROTHROMBOTIC MUTATIONS



Canonico et al, 2008

MULTITUDE OF "PHENOTYPES" AT MENOPAUSE

Giulia, 59 yrs
DYSPAREUNIA/
OAB

Rosa, 49 yrs
NO SYMPTOMS

Teresa, 54 yrs
OSTEOPOROSIS
/VVA

Carla, 52 yrs
VVA/BREAST
CANCER

Laura, 62 yrs
NO SEXUAL
ACTIVITY/HOT
-FLUSHES

Anna, 56 yrs
CVD/METS/
HSDD

RE Nappi, 2014

SIPGO
Società Italiana per la Psicosomatica in Ginecologia e Ostetricia

STATO DELL'ARTE SULLE TERAPIE IN UN'OTTICA INTEGRATA

Rossella E. Nappi

Endocrinologia Ginecologica e della Menopausa &
Centro di Ricerca per la Procreazione Medicalmente Assistita – IRCCS Fondazione Policlinico S. Matteo,
Università degli Studi di Pavia

Prevention of diseases after menopause

R. A. Lobo, S. R. Davis, T. J. De Villiers†, A. Gompel‡, V. W. Henderson**, H. N. Hodis††, M. A. Lumsden‡‡, W. J. Mack***, S. Shapiro††† and R. J. Baber‡‡‡*

CLIMACTERIC 2014;17:540–556

- **WOMEN PRESENTING TO THEIR HCPs DURING THE MENOPAUSAL TRANSITION PROVIDE A UNIQUE OPPORTUNITY FOR**

- RISK ASSESSMENT
- COUNSELLING
- INSTITUTION OF VARIOUS PREVENTION MEASURES, INCLUDING HT IF NEEDED

IL GINECOLOGO & LA PREVENZIONE PRIMARIA

RE Nappi, 2015

Prevention of diseases after menopause

R. A. Lobo, S. R. Davis, T. J. De Villiers†, A. Gompel‡, V. W. Henderson**, H. N. Hodis††, M. A. Lumsden‡‡, W. J. Mack***, S. Shapiro††† and R. J. Baber‡‡‡*

CLIMACTERIC 2014;17:540–556

- **ALL PMW SHOULD BE ENCOURAGED TO**
  - TAKE ADEQUATE CALCIUM & VITD
  - ENGAGE IN REGULAR EXERCISE
  - STOP SMOKING
  - LIMIT ALCOHOL INTAKE
  - BE CAREFUL TO REDUCE THE RISK OF FALLS

WOMEN'S CV HEALTH

AHA recommendations for
preventing heart disease
in women

Ideal cardiovascular health (all of these)

- Total cholesterol < 200 mg/dL
- BP < 120/< 80 mmHg
- Fasting blood glucose < 100 mg/dL
- Body mass index < 25 kg/m2
- Abstinence from smoking
- Physical activity at goal for adults > 20 y of age:
  ≥ 150 min/wk moderate intensity,
  ≥ 75 min/wk vigorous intensity,
  or combination Healthy (DASH-like) diet

➢ Value are intended without treatment

Mosca et al, 2011

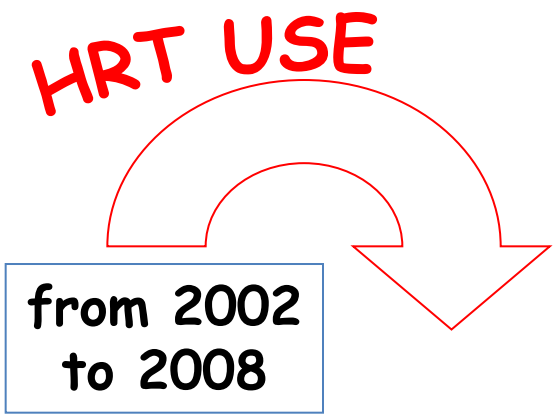
THE DROP OF HRT USE

WOMAN'S PERCEPTION

- Unnecessary medication
- Preference of a natural menopause
- Conflicting information
- Fears of side-effects
- Possible health risks

DOCTOR'S OPINION

- Patient's profile to evaluate overall therapeutic goals
- Counseling to help a woman's choice
- Individualized risk-benefit assessment
- Lowest effective dose to relieve symptoms
- Safety is essential to overcome women's fears



A REAL CHALLANGE TO GET WOMEN RECEPTIVE TO ANY KIND OF HORMONE THERAPY

RE Nappi, 2009

CRITICAL ISSUES IN HRT CHOICE

AGE & TYPE OF MENOPAUSE

Personal Experiences & Preferences

- SELECTION (Symptomatology, Timing)
- RISKS/BENEFITS BALANCE (History, Vulnerability)
- COUNSELING (Education, Support)
- INDIVIDUALIZATION (Type, Dose, Duration)
- ECONOMIC ISSUES (Costs, Follow-up)

RE Nappi, 2008

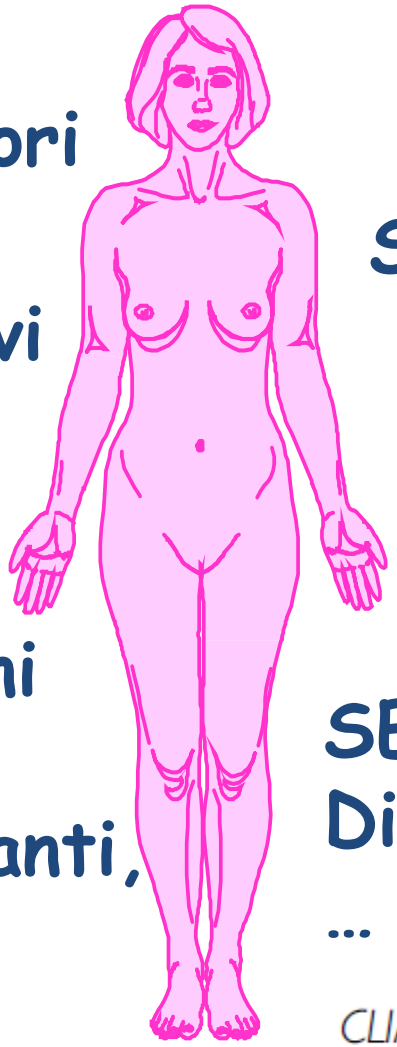
‘PROFOX’ – the post HRT nightmare

J. Studd

Fitoestrogeni,
Altri Integratori

Statine

Agenti Psicoattivi

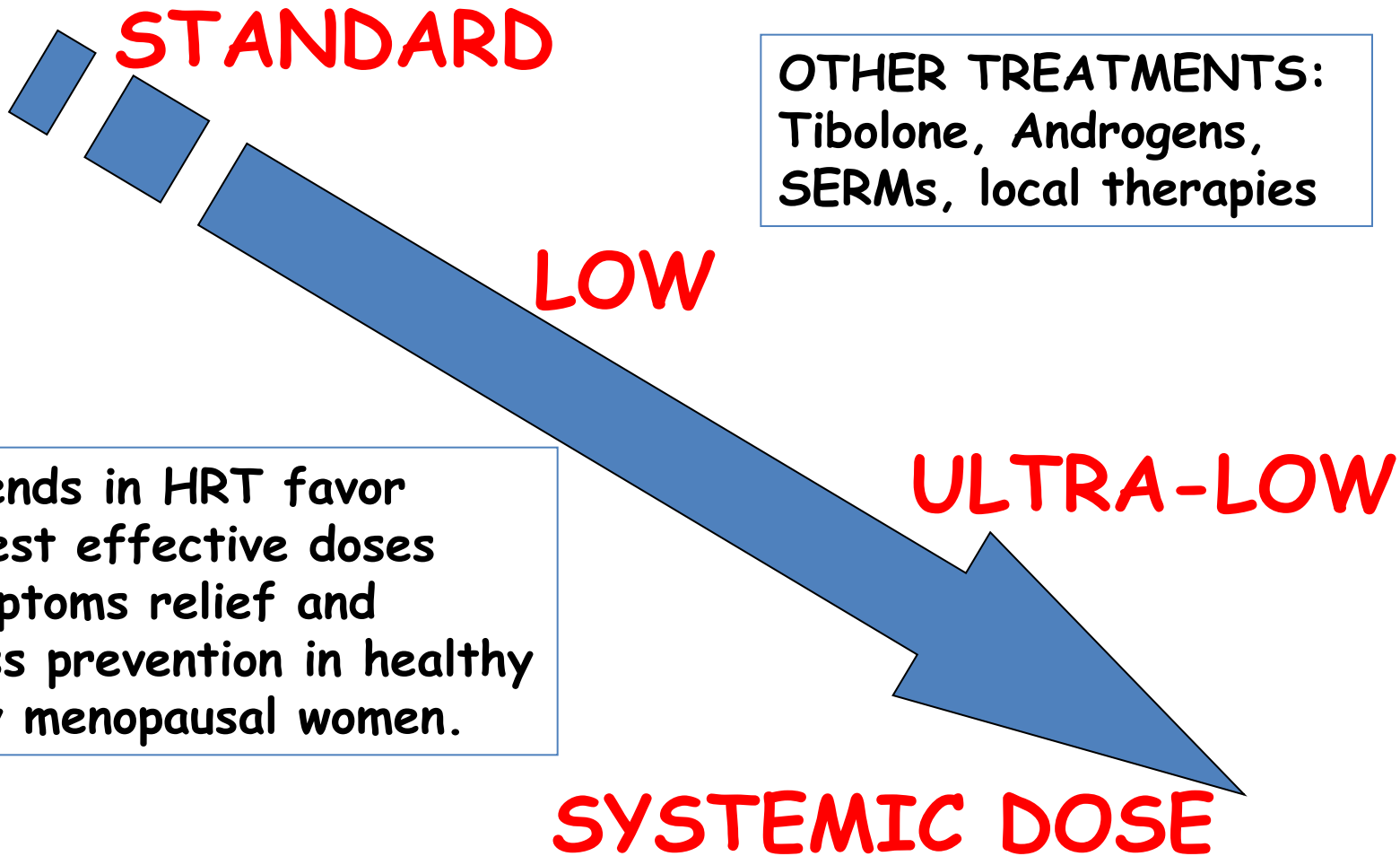


Estrogeni
Locali,
Lubrificanti,
…

SERM
Difosfonati,
…

CLIMACTERIC 2010; Early Online, 1–3

HRT: AN EVOLVING CONCEPT FOR THE INDIVIDUALIZED CARE



OTHER TREATMENTS:
Tibolone, Androgens,
SERMs, local therapies

New trends in HRT favor
the lowest effective doses
for symptoms relief and
bone loss prevention in healthy
recently menopausal women.

RE Nappi, 2008

Recommendations From International Associations Regarding Use of Hormone Therapy[1-3]

Determine patient's health priorities based on initial HT discussion

HT contraindicated

Yes

Do not recommend HT
Risk > benefit

Recommend non-hormonal vaginal lubricants/moisturizers and drugs (eg, anti-depressants) depending on specific symptoms

No

Predominantly Local Symptoms

Vaginal/urogenital symptoms?

Yes

Recommend local ET (now first-line)

Benefits >>> risks

No

Systemic Symptoms

Vasomotor symptoms? Sleep disturbance?

Yes

Recommend systemic HT (ET or EPT)

Benefits > risks

Annually re-evaluate ongoing need for therapy

No

Affected mood or depressive symptoms?

Yes

Consider very low dose ET alone or in combination with antidepressants

ET may yield benefits

Therapeutic goal: Use the lowest effective dose of estrogen consistent with treatment goals, benefits, and risks

ET = estrogen therapy; EPT = estrogen-progestogen therapy; HT = hormone therapy.

1. International Menopause Society. Climacteric. 2011;14:302-320.
2. North American Menopause Society. Menopause. 2012;19:257-271
3. North American Menopause Society. Menopause. 2013;20:888-902.

ALLEARSI CON IL GINECOLOGO

- Il ginecologo DEVE CONCORDARE con la donna il tipo di TERAPIA fornendo SPIEGAZIONI dettagliate sulla scelta e il tempo d'uso, discutendo i possibili effetti COLLATERALI e gli eventuali RISCHI, invitandola a riferire ogni singolo DISTURBO attribuibile alla terapia, pianificando gli opportuni CONTROLLI per favorire l'ACCETTABILITA'

Visite di maggior durata promuovono la compliance, riducendo i timori della donna!!!

RE Nappi, 2007

I MEDICI NON SONO TUTTI UGUALI!

AMICO

Ascoltare

Interagire/Dialogare

PSICOLOGO

Condividere informazioni

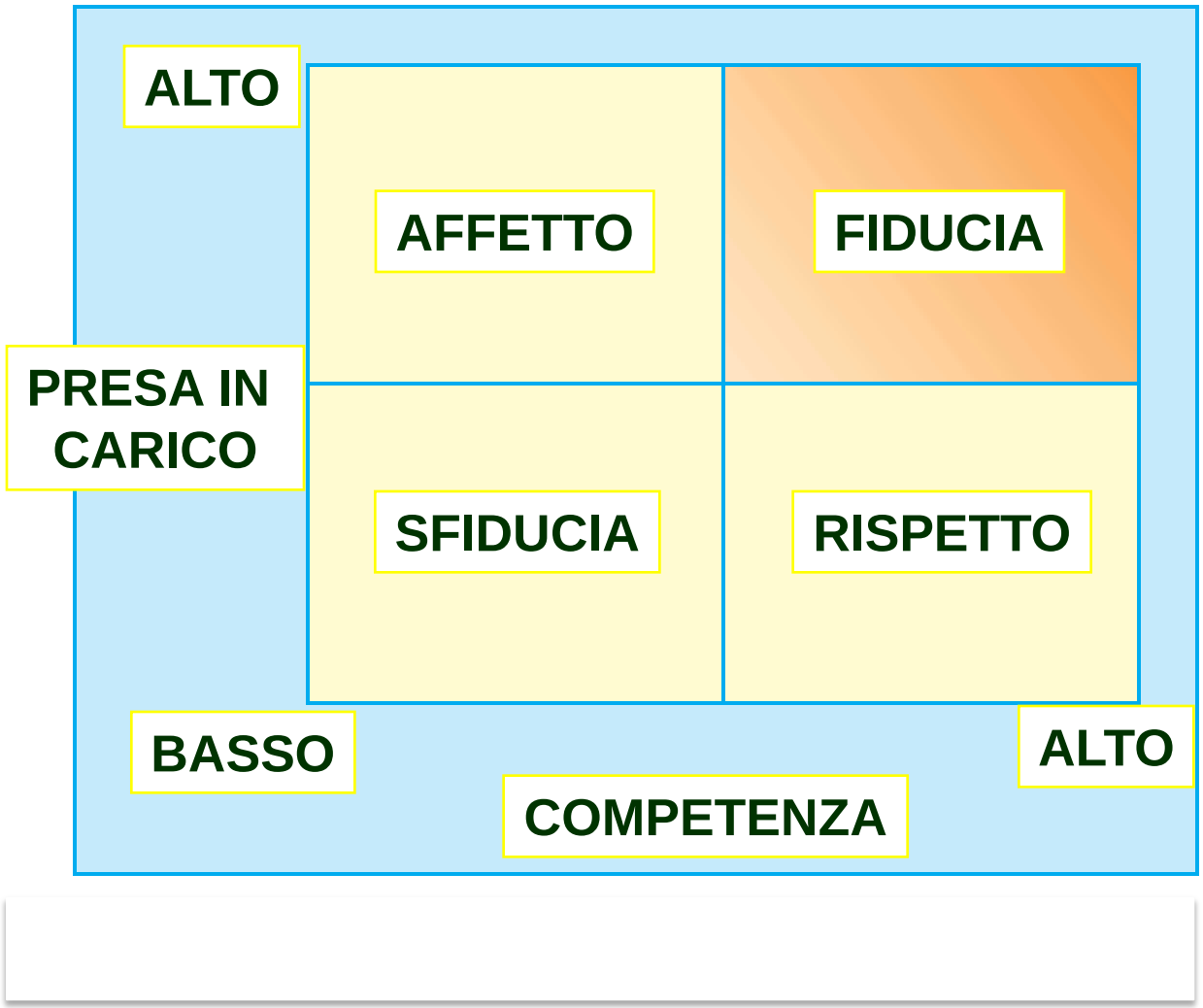
PADRE, MADRE

Fornire conoscenze ed esperienze

INSEGNANTE

Cortesia di J Bitzer, 2010

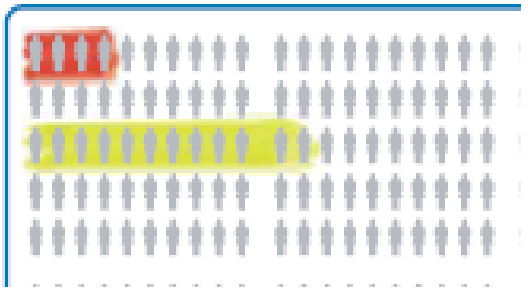
COSTRUIRE LA RELAZIONE MEDICO-PAZIENTE



Modificato da Spence, 1996

COME COMUNICARE I RISCHI

- Il modo in cui i medici comunicano i rischi può influenzare la percezione del rischio da parte delle donne
- Aggiungere dati numerici alle spiegazioni è utile, ma è meglio usare numeri assoluti e non rischio relativo o percentuali
- Utilizzare un ausilio visivo e mettere in prospettiva rischi-benefici serve a massimizzare la comprensione e a facilitare il rapporto medico-paziente
- Fare in modo che il "consenso informato" della donna sia basato sulla effettiva comprensione e non soltanto su dati statistici



J Paling, 2003

Updated IMS recommendations on postmenopausal hormone therapy and preventive strategies for midlife health

D. W. Sturdee and A. Pines on behalf of the International Menopause Society Writing Group

Writing Group: D. F. Archer, R. J. Baber, D. Barlow, M. H. Birkhäuser, M. Brincat, L. Cardozo, T. J. de Villiers, M. Gambacciani, A. A. Gompel, V. W. Henderson, C. Kluft, R. A. Lobo, A. H. MacLennan, J. Marsden, R. E. Nappi, N. Panay, J. H. Pickar, D. Robinson, J. Simon, R. L. Sitruk-Ware and J. C. Stevenson

Governing principles

- HRT should not be recommended without a clear indication for its use, i.e. significant symptoms or physical effects of estrogen (androgen) deficiency.
- Postmenopausal HRT is not a single regimen given to a standard woman.
- HRT must be individualized and tailored according to symptoms and the need for prevention, as well as personal and family history, results of relevant investigations, the woman's preferences and expectations.

Climacteric 2011;14:302–20.

IMS-initiated Workshop, Paris, Nov 2012

Global Consensus

IMS updated recommendations

Endorsed by NAMS, APMF, EMAS, ASRM, IOF, the Endocrine Society

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass, C. J. Haines, J. E. Hall, R. A. Lobo, D. D. Pierroz and M. Rees

CLIMACTERIC 2013;16:203–204

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass[ς], C. J. Haines[†], J. E. Hall[‡], R. A. Lobo[ς ς], D. D. Pierroz[††] and M. Rees[‡‡]

CLIMACTERIC 2013;16:203–204

Governing principles

- **HRT must be individualized and tailored according to symptoms and the need for prevention, as well as personal and family history, results of relevant investigations, the woman's preferences and expectations.**

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass[c], C. J. Haines[†], J. E. Hall[‡], R. A. Lobo[c c], D. D. Pierroz[††] and M. Rees[‡‡]

CLIMACTERIC 2013;16:203–204

Governing principles

- **The option of MHT is an individual decision in terms of quality of life and health priorities as well as personal risk factors such as age, time since menopause and the risk of venous thromboembolism, stroke, ischemic heart disease and breast cancer.**

Global Consensus Statement on Menopausal Hormone Therapy

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CLIMACTERIC 2013;16:203–204

Governing principles

- **The dose and duration of MHT should be consistent with treatment goals, such as symptom relief, and should be individualized.**

Global Consensus Statement on Menopausal Hormone Therapy

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CLIMACTERIC 2013;16:203–204

Governing principles

- **Local low-dose estrogen therapy is preferred for women whose symptoms are limited to vaginal dryness or associated discomfort with intercourse.**

In addition to relief of vaginal symptoms, low-dose vaginal estrogen has also been shown to alleviate sensory urgency and reduce the frequency of urinary tract infections.

The use of hormone therapy for the maintenance of urogynecological and sexual health post WHI

ABSTRACT

Background The loss of estrogen at menopause and the gradual decline in testosterone with age are associated with urogenital atrophy and, as a result, urogenital tract symptoms, including lower urinary tract symptoms and dyspareunia. These symptoms will persist unless treated.

Objective To review the prevalence of urogenital tract symptoms and sexual health problems associated with menopause and the role in the use of hormone therapy for the treatment of symptomatic women, with a specific focus on what has been learned since the first publication of the Women's Health Initiative (WHI) estrogen and estrogen + progestin studies.

Conclusion Studies support the use of local estrogen therapy, but not systemic estrogen therapy, for the treatment of urge urinary incontinence, overactive bladder and to reduce the number of urinary tract infections. The current evidence does not favor a beneficial effect on stress urinary incontinence. Local estrogen therapy is effective for the treatment of dyspareunia caused by vulvovaginal atrophy. Preliminary studies suggest a potential role for both intravaginal dehydroepiandrosterone and testosterone in the treatment of dyspareunia secondary to vulvovaginal atrophy, however, confirmatory studies are required before either therapy can be recommended. Post WHI, there is a need for medical practitioners to proactively raise the topic of urogynecological and sexual health in order to discuss the most suitable treatment option.

Nappi & Davis, 2012

Recommendations for the management of postmenopausal vaginal atrophy

D. W. Sturdee and N. Panay, on behalf of the International Menopause Society Writing Grout*

18th October 2010 – World Menopause Day

ENDING THE SILENT SUFFERING

Managing Vaginal Atrophy in Postmenopausal Women

SAVE THE DATE

Restoration of urogenital physiology

Alleviation of symptoms

- Systemic HRT relieves vaginal atrophy in about 75% of women.
- Combination of systemic and local therapy may be required initially for some women.

Local estrogen therapy

Although systemic estrogen therapy will treat vaginal atrophy, local vaginal estrogen therapy is preferable, when systemic treatment is not needed for other reasons, because local therapy avoids most systemic adverse events and is probably also more efficacious for vaginal problems.

Local estrogen therapy can be given as tablets, pessaries/vagitories, cream or a vaginal ring. [The terms 'pessaries' and 'vagitories' are synonymous.] Therapy is available as conjugated equine estrogens, estradiol, estriol or estrone.

- All currently available topical estrogens are absorbed, the extent depending on dose and formulation.

- Treatment should be started early and before irrevocable atrophic changes have occurred.
- Treatment needs to be continued to maintain the benefits.
- All local estrogen preparations are effective and patient preference will usually determine the treatment used.

- Long-term use of low-dose topical vaginal estrogen preparations is not contraindicated.

CLIMACTERIC 2010;13:509–522

Recommendations for the management of postmenopausal vaginal atrophy

D. W. Sturdee and N. Panay, on behalf of the International Menopause Society Writing Grout*

Non-hormonal treatment/lubricants

Lubricants and non-hormonal treatments for vaginal atrophy mainly consist of a combination of protectants and thickening agents in a water-soluble base and non-hormonal substances that have a maturation effect on the urogenital epithelium. Lubricants are primarily used to relieve vaginal dryness during intercourse and therefore do not provide a long-term solution. There are some data suggesting that moisturizers and some other substances may have a longer-lasting effect if used consistently. Non-hormonal options are primarily indicated in women wishing to avoid hormonal therapy or in high-risk individuals with a history of hormone-sensitive malignancy such as breast or endometrial cancer. Most of these products are available without prescription over the counter and can be expensive.

Lubricants Lubricants are non-physiological, giving only a very temporary relief of symptoms, often followed by vaginal irritation. Vaseline can break down the latex of condoms.

18th October 2010 – World Menopause Day

ENDING THE SILENT SUFFERING

Managing Vaginal Atrophy in Postmenopausal Women

SAVE THE DATE

Moisturizers Moisturizers are hydrophilic, insoluble, cross-linked polymers. They are bio-adhesive in that they attach to mucin and epithelial cells on the vaginal wall, thus retaining water. They are eliminated by epithelial cell turnover. The beneficial effects on symptoms related to vaginal atrophy are mainly through buffering properties which lead to a reduction in vaginal pH. Cytomorphometric analysis of vaginal smears in 38 postmenopausal women has shown an increase in mean cellular area, indicating a positive effect on the maturation of the vaginal epithelium. However, there is no effect on the overall maturation value/index[37].

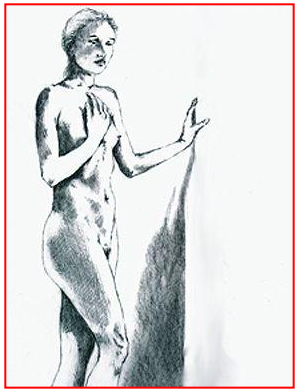
The efficacy on vaginal symptoms is lower than that of topical estrogen therapy in the trials published thus far.

CLIMACTERIC 2010;13:509–522

International Menopause Society
promoting education and research on all aspects of adult women's health
www.imsociety.org

INTEGRATED BIO-PSYCHOLOGICAL APRROACH TO VVA IN WOMEN WITH CONTRAINDICATIONS TO LOCAL HORMONAL PRODUCTS

- EDUCATION ON BODY/GENITAL AWARENESS
- SELF-MASSAGE WITH EUTROPHIC PRODUCTS
- PELVIC FLOOR EXERCISES/ LASER TREATMENT
- MOISTURIZERS/LUBRICANTS
- PSYCHO-SEXUAL COUNSELLING



RE Nappi, 2013

Global Consensus Statement on Menopausal Hormone Therapy

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CLIMACTERIC 2013;16:203–204

Governing principles

- **In women with premature ovarian insufficiency, systemic MHT is recommended until the average age of the natural menopause.**

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CLIMACTERIC 2013;16:203–204

Governing principles

- **MHT includes a wide range of hormonal products and routes of administration, with potentially different risks and benefits. Thus, the term ‘ class effect ’ is confusing and inappropriate.**
- **However, evidence regarding differences in risks and benefits between different products is limited.**

Global Consensus Statement on Menopausal Hormone Therapy

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CLIMACTERIC 2013;16:203–204

Governing principles

- **Women taking HRT should have at least an annual consultation to include a physical examination, update of medical and family history, relevant laboratory and imaging investigations, a discussion on lifestyle, and strategies to prevent or reduce chronic disease. There is currently no indication for increased mammographic or cervical smear screening.**

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass[ε], C. J. Haines[†], J. E. Hall[‡], R. A. Lobo[εε], D. D. Pierroz[††] and M. Rees[‡‡]

CLIMACTERIC 2013;16:203–204

Benefits of MHT

- **MHT is the most effective treatment for moderate to severe menopausal symptoms and is most beneficial before the age of 60 years or within 10 years after menopause.**

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass[c], C. J. Haines[†], J. E. Hall[‡], R. A. Lobo[c c], D. D. Pierroz[††] and M. Rees[‡‡]

CLIMACTERIC 2013;16:203–204

Benefits of MHT

- **Other menopause-related complaints, including arthralgia and muscle pains, depression, sleep disturbances and vaginal atrophy, may improve during MHT. The administration of individualized MHT (including androgenic preparations when appropriate) may improve both sexuality and overall quality of life.**

Global Consensus Statement on Menopausal Hormone Therapy

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CLIMACTERIC 2013;16:203–204

MHT & Bone

- **In postmenopausal women at risk of fracture and younger than 60 years, or within 10 years of menopause, MHT can be considered as one of the first-line therapies for the prevention and treatment of osteoporosis related fractures.**

MHT is an effective treatment for the prevention of fracture in at-risk women before age 60 years or within 10 years after menopause.

Global Consensus Statement on Menopausal Hormone Therapy

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CLIMACTERIC 2013;16:203–204

MHT & CVD

- **RCT and observational data provide strong evidence that standard-dose estrogen-alone MHT decreases coronary disease and all-cause mortality in women younger than 60 years of age and within 10 years of menopause.**
- **Data on estrogen – progestogen therapy in this population show a similar trend but with less precision.**

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CLIMACTERIC 2013;16:203–204

MHT & CVD

- **Initiation of MHT in elderly women or those who are more than 10 years postmenopause may be associated with increased risk for coronary events, mainly in the first 2 years of use.**
- **It is therefore not recommended to initiate MHT beyond the age of 60 years solely for the purpose of primary prevention of CAD.**

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass[ε], C. J. Haines[†], J. E. Hall[‡], R. A. Lobo[εε], D. D. Pierroz[††] and M. Rees[‡‡]

CLIMACTERIC 2013;16:203–204

MHT & Breast Cancer

- **The degree of association between breast cancer and postmenopausal MHT remains controversial.**
- **Randomized controlled data from the WHI study demonstrated no increased risk in first-time users of combined MHT during the 5 – 7 years since initiation of treatment.**
- **7.1 years of treatment with unopposed CEE decreased the risk of breast cancer diagnosis and mortality in hysterectomized women.**

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass, C. J. Haines, J. E. Hall, R. A. Lobo, D. D. Pierroz and M. Rees

CLIMACTERIC 2013;16:203–204

MHT & Breast Cancer

- **The risk of breast cancer in women over 50 years associated with MHT is a complex issue.**
- **The risk of breast cancer attributable to MHT is small and the risk decreases after treatment is stopped.**
- **The increased risk of breast cancer is primarily associated with the addition of a progestogen to estrogen therapy and related to the duration of use.**

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass*, C. J. Haines†, J. E. Hall‡, R. A. Lobo**, D. D. Pierroz†† and M. Rees‡‡

CLIMACTERIC 2013;16:203–204

MHT & Thromboembolism

- **The risk of venous thromboembolic events and ischemic stroke increases with oral MHT but the absolute risk is rare below age 60 years.**
- **Observational studies point to a lower risk with low-dose transdermal therapy.**

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass[ε], C. J. Haines[†], J. E. Hall[‡], R. A. Lobo[εε], D. D. Pierroz[††] and M. Rees[‡‡]

CLIMACTERIC 2013;16:203–204

MHT & Compounded Hormones

- **The use of custom compounded bioidentical hormone therapy is not recommended.**

Tibolone in postmenopausal women: a review based on recent randomised controlled clinical trials

NICOLETTA BIGLIA[1], SILVIA MAFFEI[2], STEFANO LELLO[3], & ROSSELLA E. NAPPI[4,5]

- Selective
- Tissue
- Estrogenic
- Activity
- Regulator

·Estrogenic, progestogenic, androgenic properties
·SERM profile achieving biological effects without directly modulating the estrogen, androgen, or progesterone receptors
·Various metabolites exert their effects directly on these receptors or by modulating endogenous steroid activity within different tissues

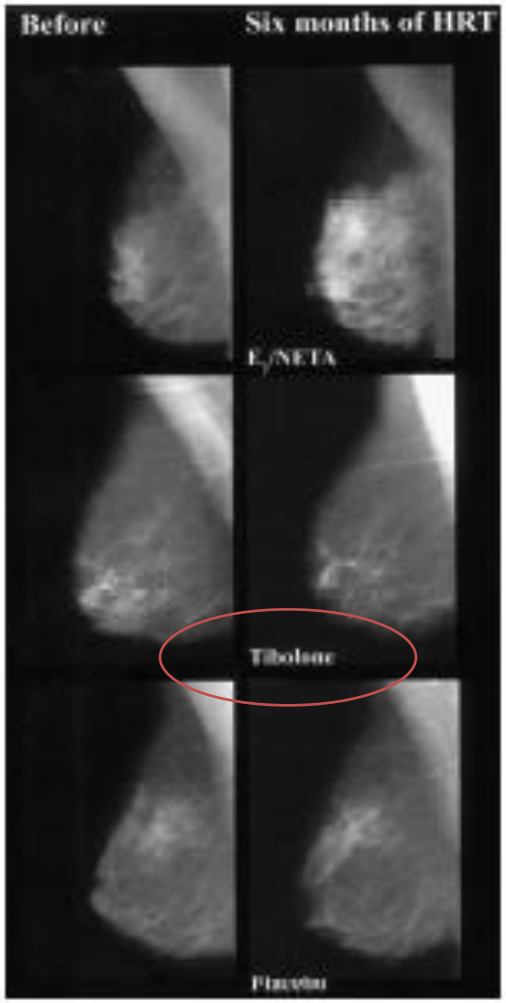
Abstract

Aim. To critically discuss the use of tibolone (T), in light of a series of very recent double-blind placebo (PL) controlled trials (LISA, LIFT, OPAL, THEBES, LIBERATE) conducted worldwide in a large number of postmenopausal women (PMW).

Methods. The most relevant publications on T therapy in PMW were considered with emphasis on menopausal symptoms, quality of life, sexuality, bone, cardiovascular system (CVS) and oncologic risk.

Results. T significantly relieves climacteric symptoms and improves mood and sexual well-being (LISA). T is as effective as estrogen–progestin therapy in preventing bone loss and reducing the relative risk of vertebral and non-vertebral fractures (LIFT). By using surrogate endpoints of the individual risks for the CVS, studies show mixed results, but a favourable effect on acute miocardial infarction and thromboembolism has been documented (THEBES, LIFT, OPAL). Although findings about endometrial and colon cancer are reassuring, conclusive data on breast cancer risk with T are not available and an increased risk of recurrence in women with previous breast cancer emerged (LIBERATE).

Conclusions. T is effective in treating menopausal syndrome with a good tolerability profile. In spite of some unsolved issues in term of safety, T is still a good treatment option for early PMW.



Lundstrom et al, 2002

Gynecol Endocrinol, 2010

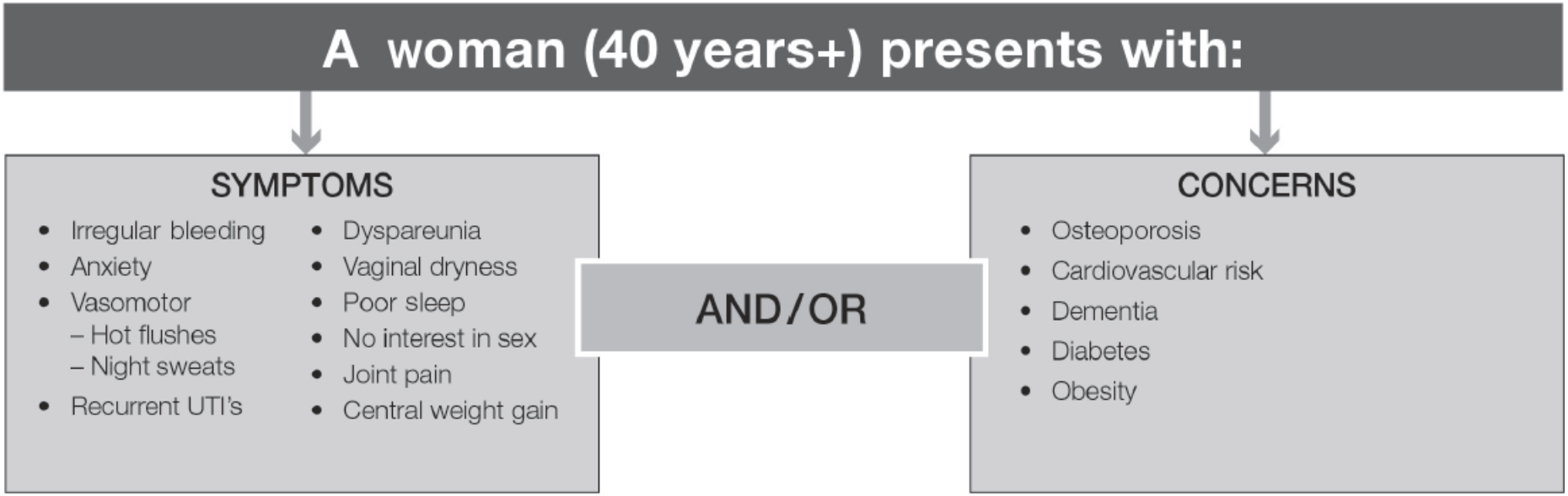
UNA VISITA “CENTRATA” SULLA DONNA

A fronte di una medicina sempre più “scientifica” ed “economicizzata”, il momento magico medico-paziente deve sopravvivere…
...non pratichiamo medicina molecolare o virtuale!

“Quando la porta si chiude e sono con la mia paziente è ancora un evento speciale, come lo è sempre stato.
Essere un medico è un privilegio e un piacere che sopravviverà…” ***Speroff, 1999***

A Practitioner's Toolkit for Managing the Menopause (1)

F. M. Jane and S. R. Davis



CLIMACTERIC 2014;17:1–16

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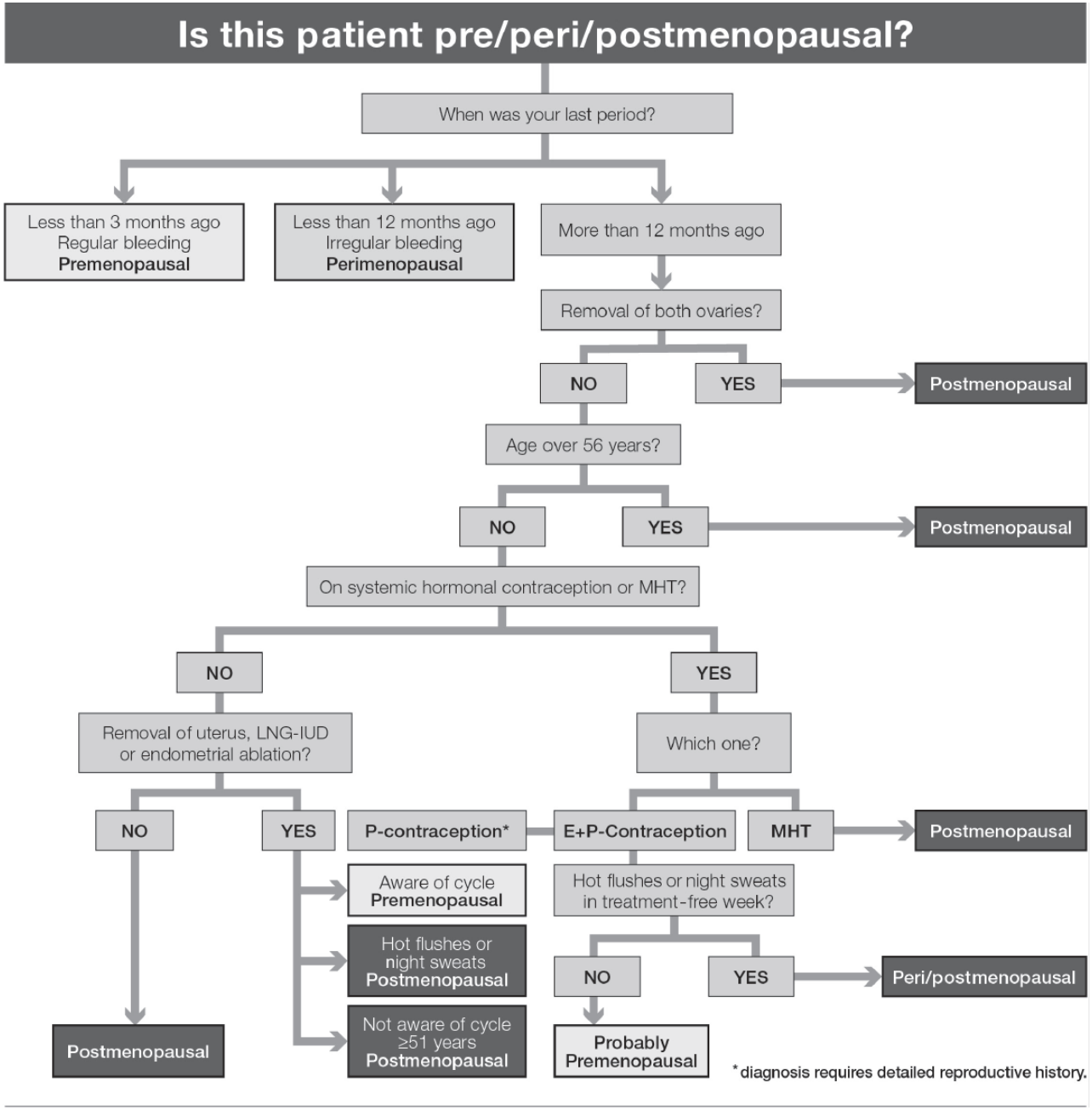

CLIMACTERIC 2014;17:1–16

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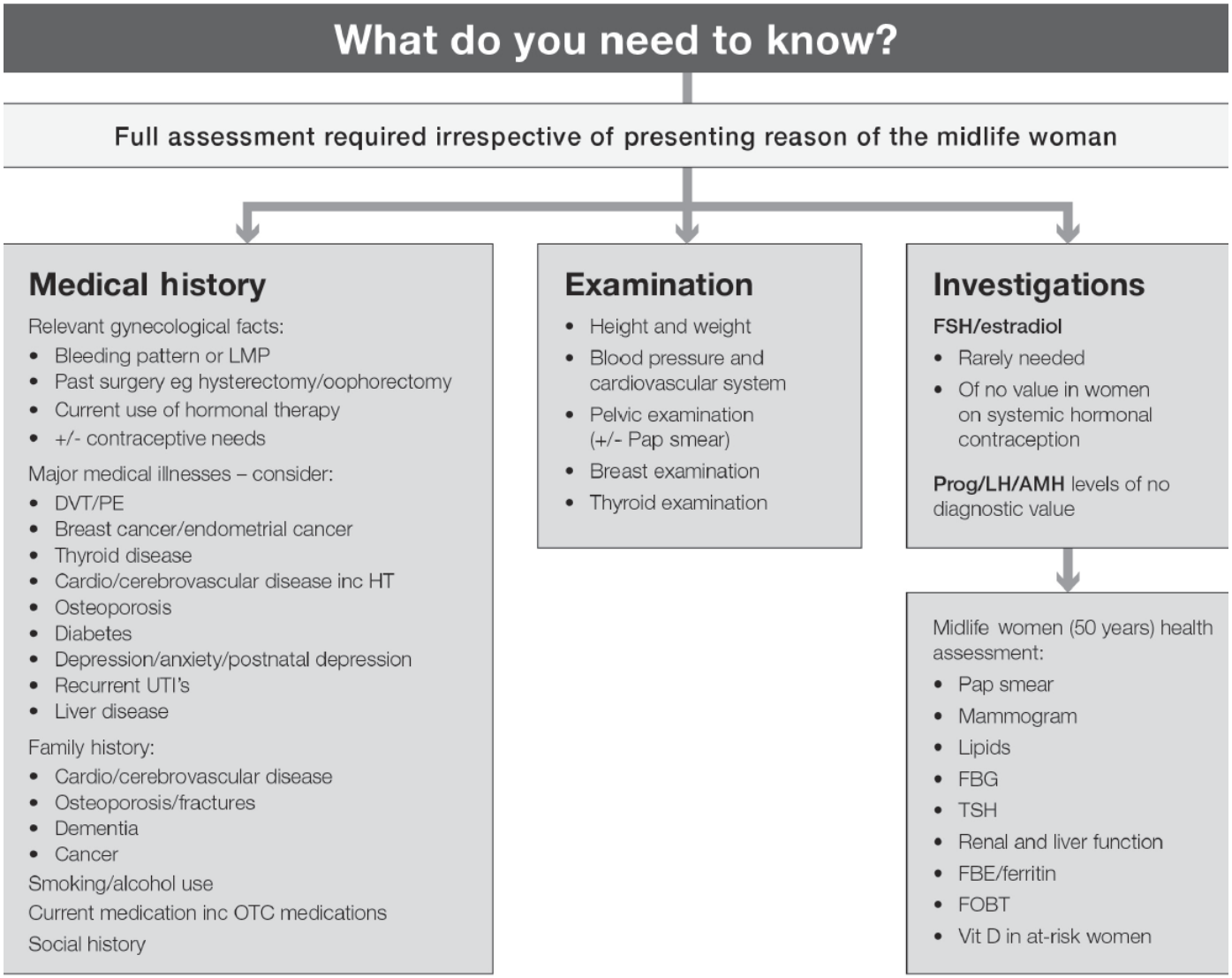

CLIMACTERIC 2014;17:1–16

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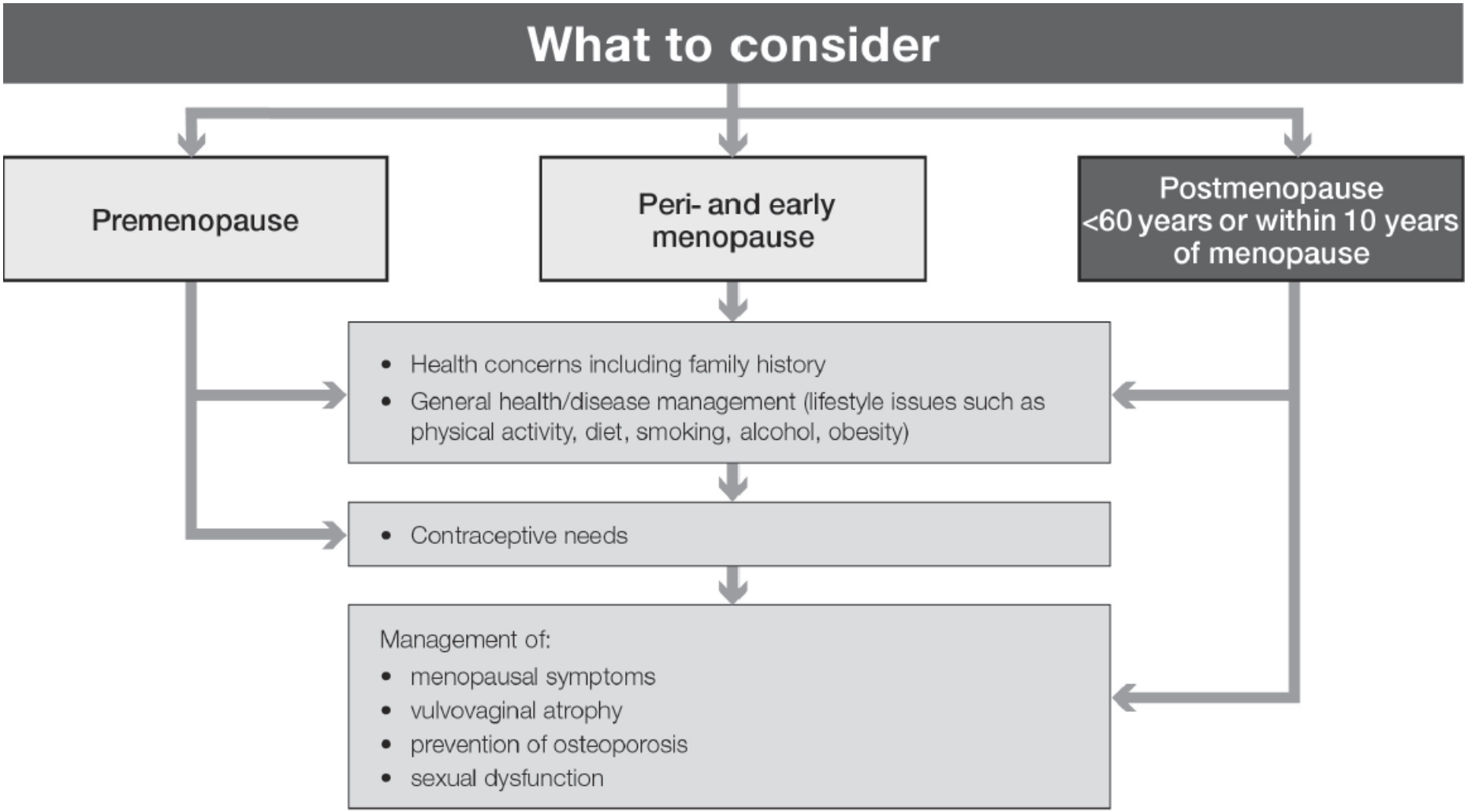

CLIMACTERIC 2014;17:1–16

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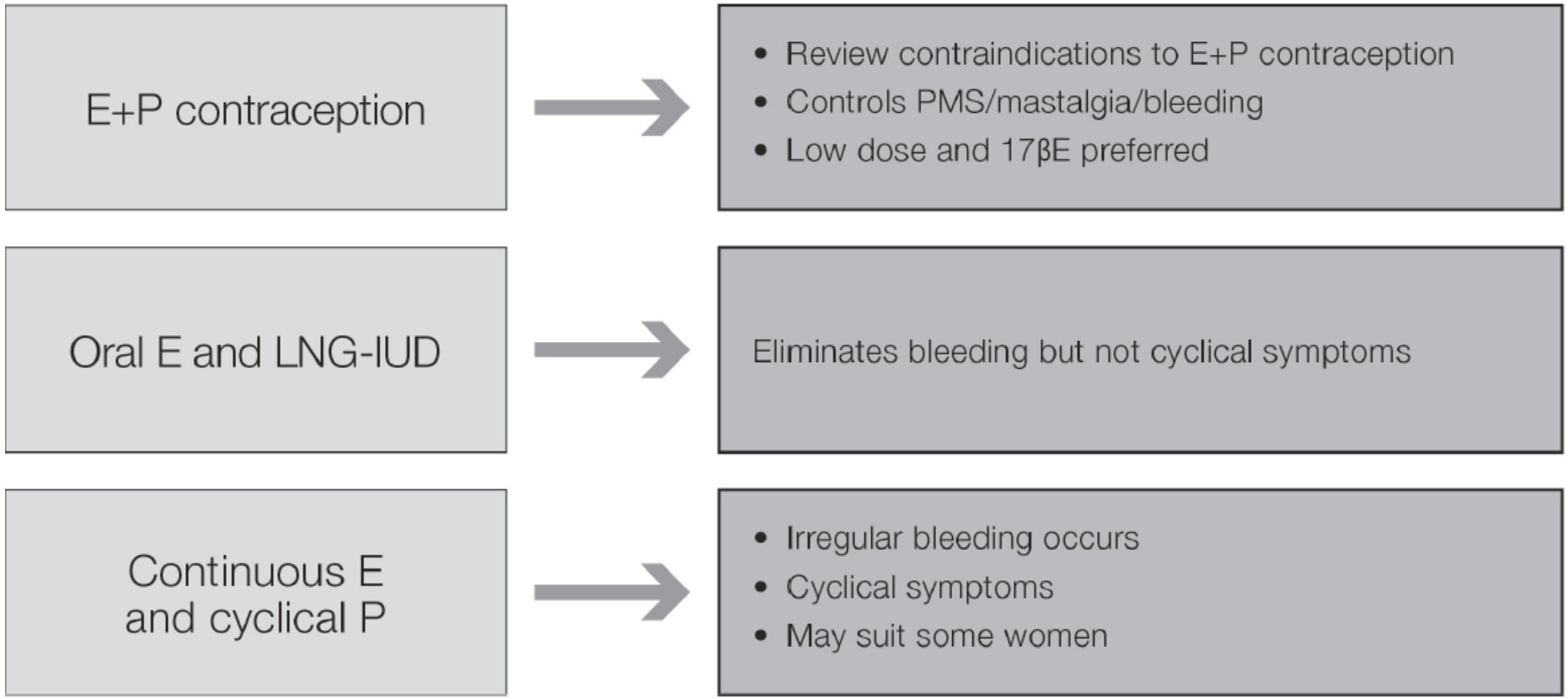
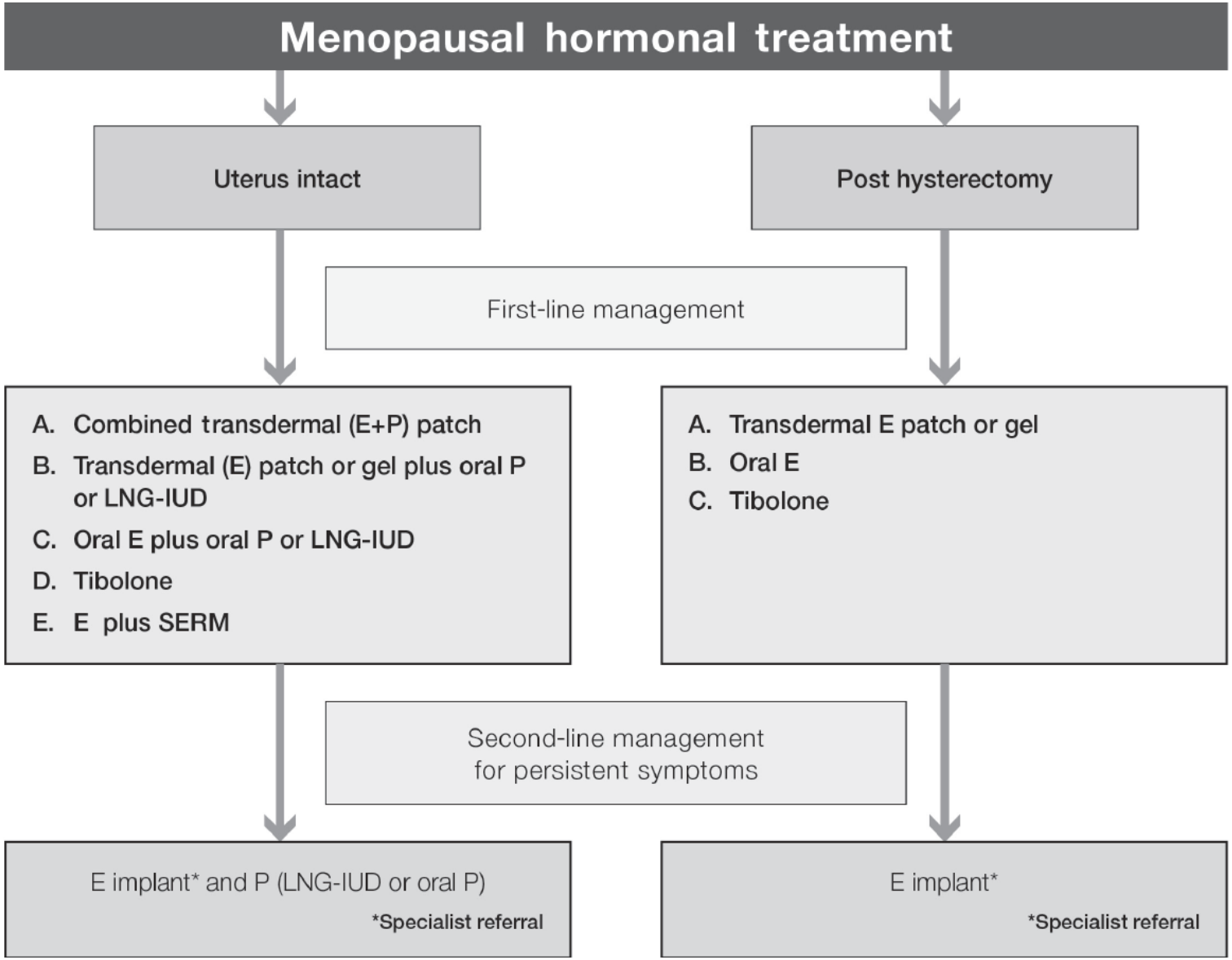
Perimenopausal treatment



CLIMACTERIC 2014;17:1–16



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CLIMACTERIC 2014;17:1–16

MHT dosing[1]

Estrogen

	Low dose	Moderate dose	High dose
CEE	0.3–0.45 mg/day	0.625 mg/day	1.25 mg/day
17β-estradiol	0.5 –1.0 mg/day	1.5–2 mg/day	2 mg
Estradiol valerate	0.5 mg/day	1 mg/day	2 mg/day
Transdermal estradiol patch	25–37.5 µg/day	50 µg/day	75–100 µg/day
Estradiol hemihydrate gel	0.5 mg/day	1.0 mg/day	1.5 mg/day

Sequential P – daily dose for 14 days per month- lowest "safe" dose with:

	Low dose E	Moderate to high dose E
Dydrogesterone	5 mg	10 mg
Micronized progesterone	100 mg	200 mg
MPA	5 mg	5–10 mg
Norethisterone acetate (NETA)	1.25 mg	1.25–2.5 mg

Continuous P – daily dose – lowest "safe" dose with:

	Low dose E	Moderate to high dose E
Dydrogesterone	5 mg	5–10 mg
Drospirenone	0.5 mg	—
Micronized progesterone	100 mg	100 mg
MPA	2.5 mg	2.5–5 mg
Norethisterone acetate (NETA)	0.5–1.0 mg	>1.0–2.5 mg
LNG-IUD	device releasing 20 µg/24 hours	

Tibolone

Tibolone	2.5 mg daily

CLIMACTERIC 2014;17:1–16

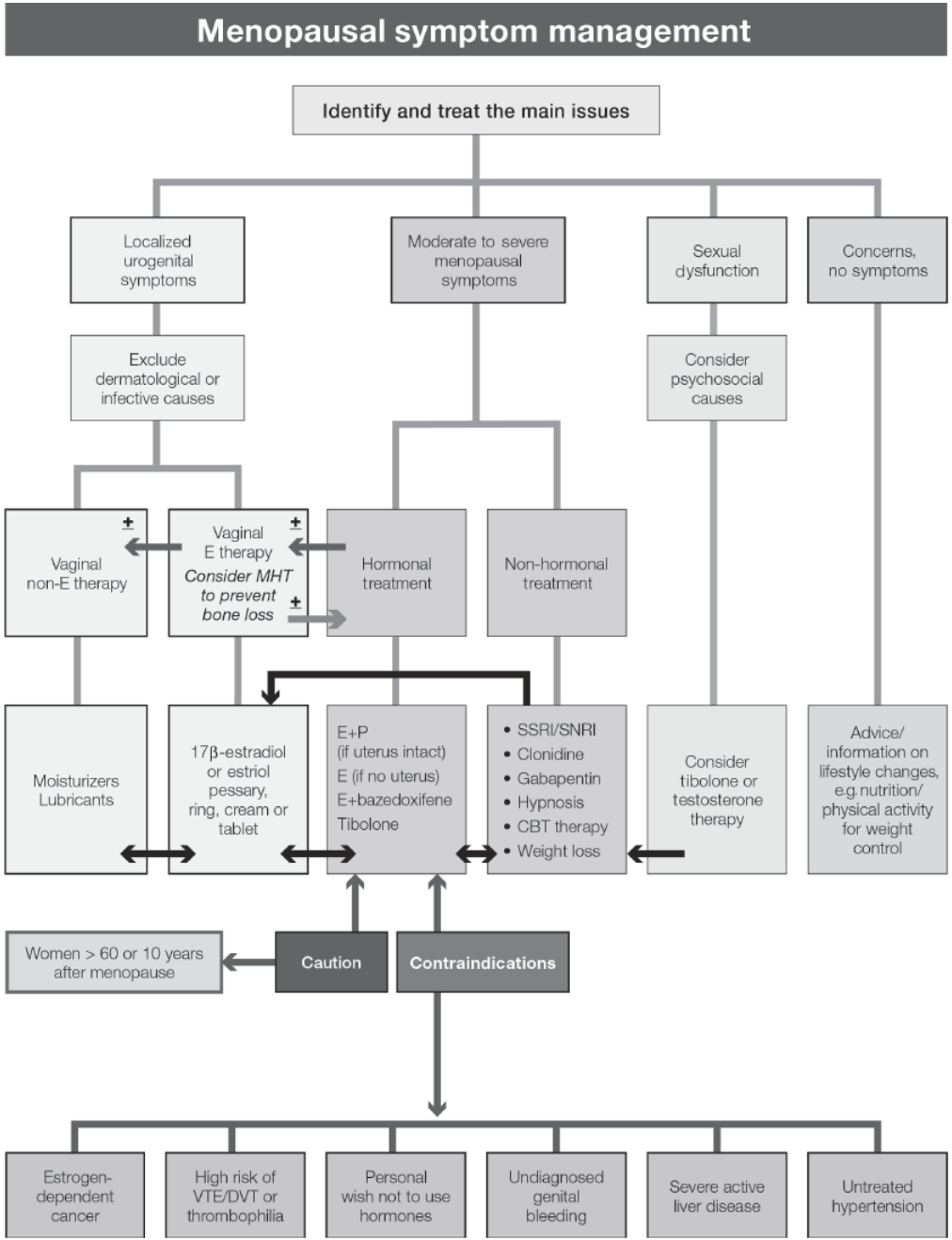
Evidence-based non-hormonal treatment [1] for vasomotor symptoms

Estrogen and SERM therapy

CEE 0.45 mg plus bazedoxifene	20 mg daily

SSRI or SSRI/SNRI– low dose (also treats menopausal mood disorder)	Venlafaxine 75mg, desvenlafaxine 50mg, escitalopram 10 mg, paroxetine 7.5 mg daily
Clonidine	100 µg daily
Gabapentin	300 – 900 mg daily
Pregabalin	75 – 150 mg twice a day
Hypnosis	
Cognitive behavior therapy	
Weight loss for obese women	
Stellate ganglion blockade*	Severe resistant VMS *specialist referral

[1] – Availability of hormonal/nonhormonal treatment and indications for use from regulatory bodies vary between countries.



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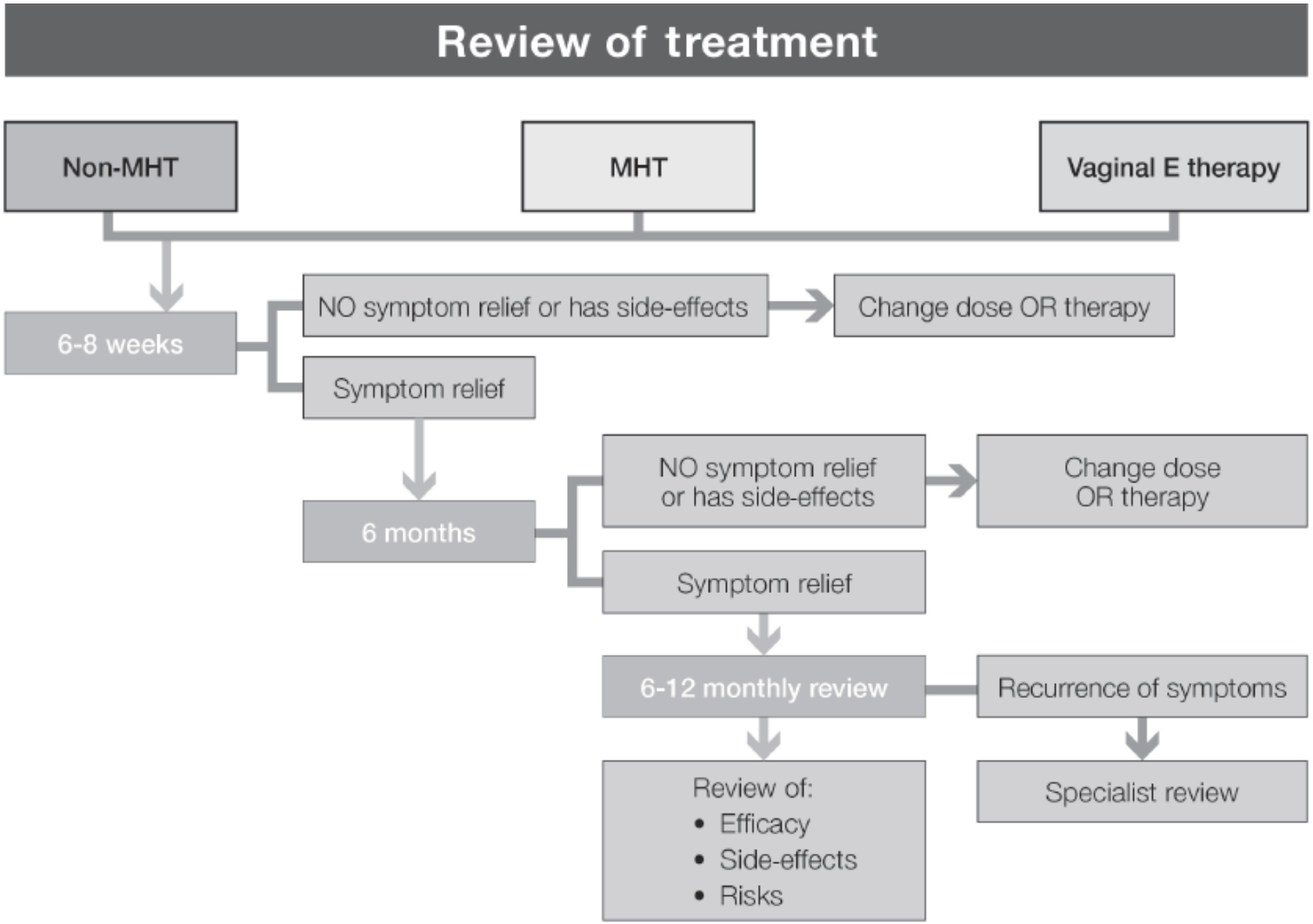

Review of treatment
Non-MHT
MHT
Vaginal E therapy
6-8 weeks
NO symptom relief or has side-effects
Change dose OR therapy
Symptom relief
6 months
NO symptom relief or has side-effects
Change dose OR therapy
Symptom relief
6-12 monthly review
Recurrence of symptoms
Review of:
• Efficacy
• Side-effects
• Risks
Specialist review

SIPGO
Società Italiana per la Psicosomatica in Ginecologia e Ostetricia

VISITIAMO INSIEME: DALLA TEORIA ALL PRATICA

Rossella E. Nappi/TEAM ENDOGIN

Endocrinologia Ginecologica e della Menopausa &
Centro di Ricerca per la Procreazione Medicalmente Assistita – IRCCS Fondazione Policlinico S. Matteo, Università degli Studi di Pavia

MULTITUDE OF "SEXUAL PHENOTYPES" AT MENOPAUSE

Giulia, 59 yrs
DYSPAREUNIA

Laura, 62 yrs
NO SEXUAL ACTIVITY

Teresa, 54 yrs
LOW DESIRE (HSDD)

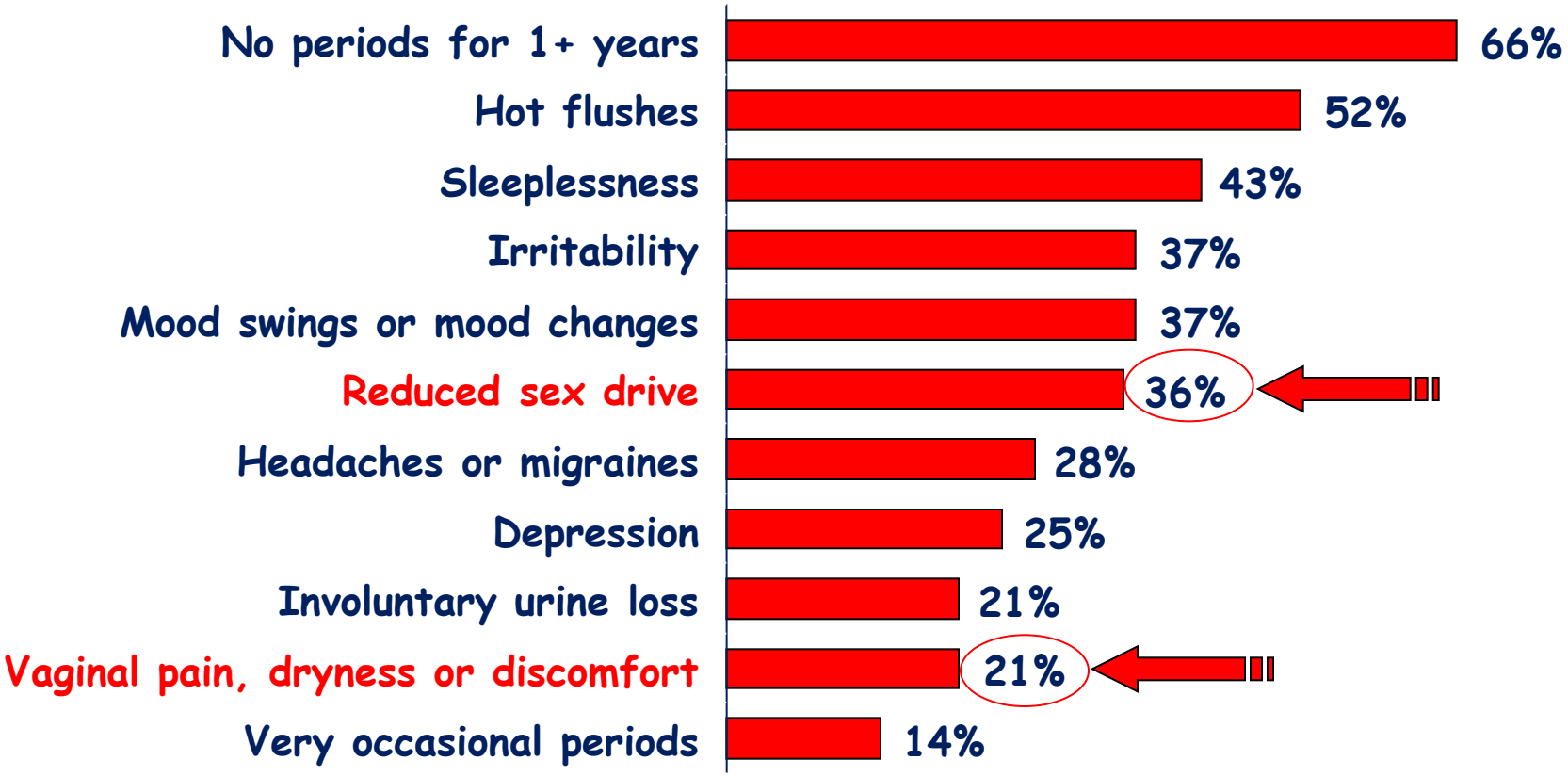
Carla, 52 yrs
VVA, BREAST CANCER

Rosa, 49 yrs
NO SEXUAL SYMPTOMS

Anna, 56 yrs
LOW DESIRE, VVA, partner ED

RE Nappi, 2014

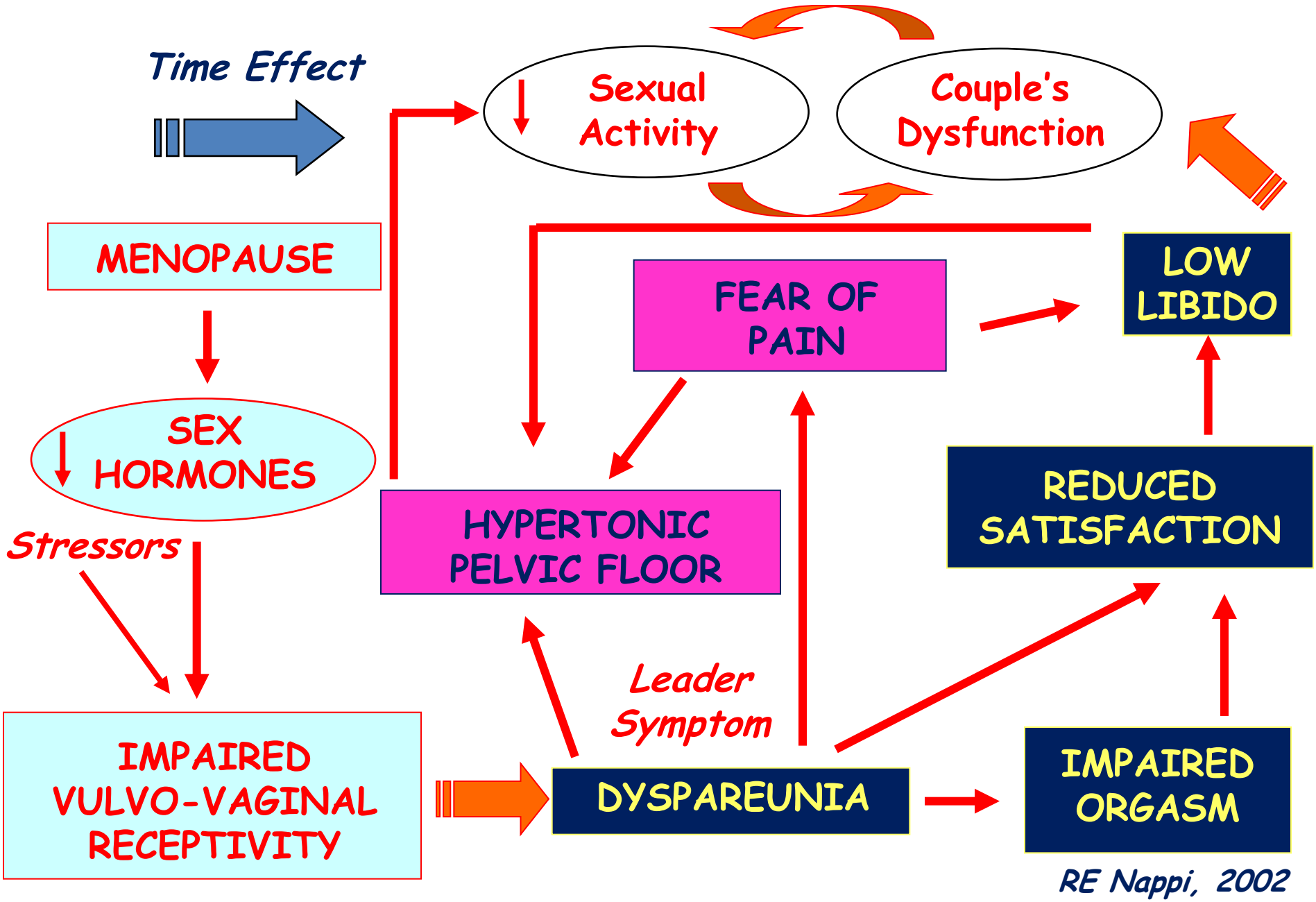
RELEVANCE OF SEXUAL ISSUES AT MENOPAUSE

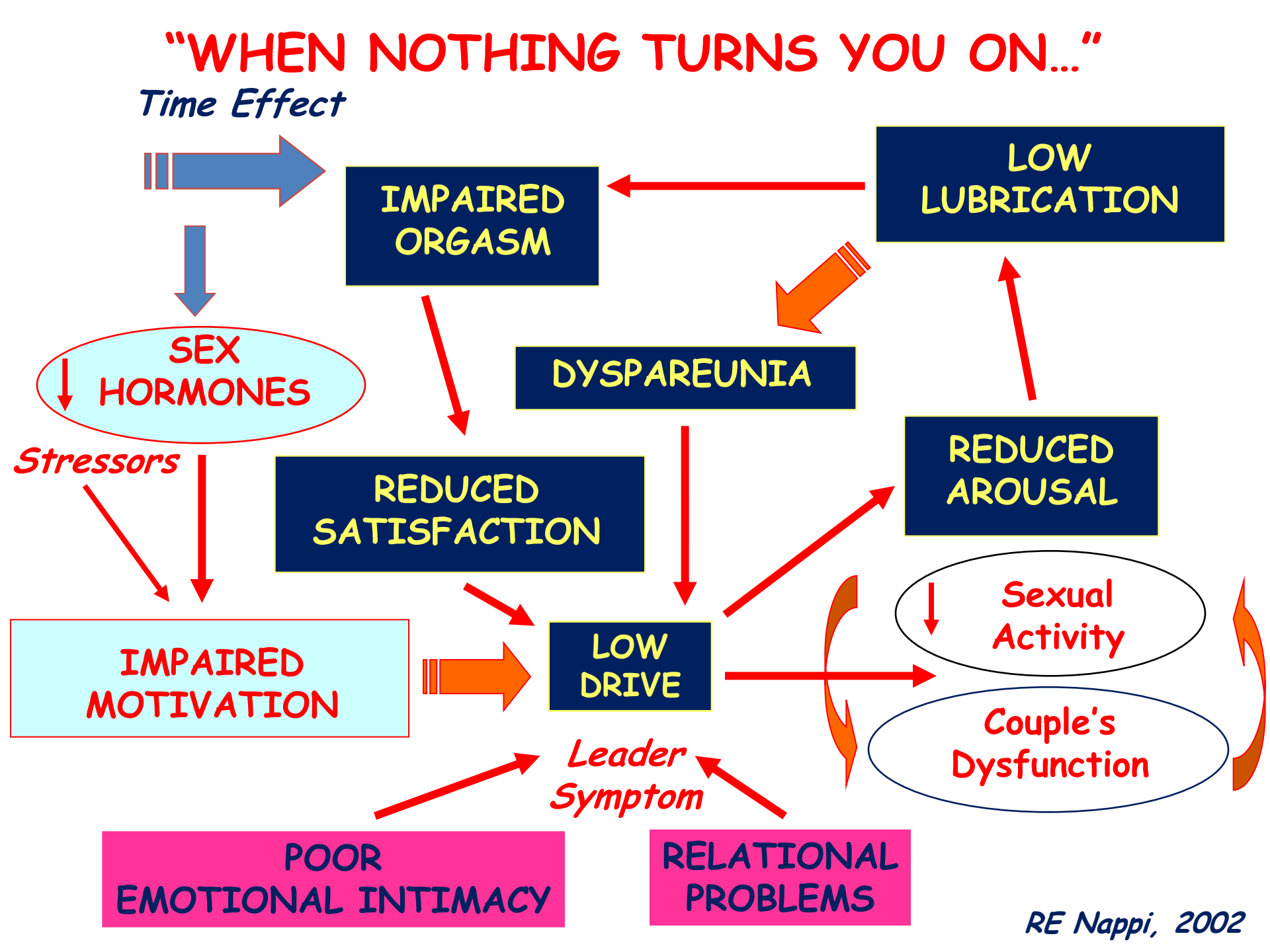


Q2A Are you currently experiencing or have you experienced any of the following in the past year?
Base: Total Sample (n=1805) of European (from Italy, Switzerland, UK, Germany, France, The Netherlands) menopausal women (age: 50-60 yrs) interviewed by phone

Nappi & Nijland, 2008

"WHEN SEX HURTS YOU..."




"WHEN NOTHING TURNS YOU ON..."
Time Effect
IMPAIRED ORGASM
LOW LUBRICATION
SEX HORMONES
DYSPAREUNIA
Stressors
REDUCED SATISFACTION
REDUCED AROUSAL
IMPAIRED MOTIVATION
LOW DRIVE
Sexual Activity
Couple's Dysfunction
Leader Symptom
POOR EMOTIONAL INTIMACY
RELATIONAL PROBLEMS
RE Nappi, 2002

ASSOCIATION OF VULVO-VAGINAL ATROPHY (VVA) WITH FSD IN POSTMENOPAUSE

Sexually active postmenopausal women (N =1,480) from The Menopause Epidemiology Study, a cross-sectional, population-based study of women 40 to 65 years old in the US chosen from a source population selected by random digit dialing and probability sampling.

- Vulvo-Vaginal Atrophy (VVA) was defined as one or more of the following: vaginal dryness, itching, irritation; pain on urination; or pain or bleeding on intercourse.
- The Arizona Sexual Experience Survey was used to define FSD.

Prevalence

- **Vulvo-Vaginal Atrophy (VVA)** **57%**
- **Female Sexual Dysfunction (FSD)** **55%**

Women with **FSD** were **3.84** times more likely to have **VVA** than women without **FSD** (95% CI: 2.99-4.94).

Levine et al, 2008

OTHER CAUSES OF SEXUAL DYSFUNCTION AT MENOPAUSE

ORGANIC

- MEDICAL DISORDERS
- SURGERY/BREAST CANCER
- DRUGS
- MENTAL HEALTH

PSYCHOLOGICAL

- HISTORY OF TRAUMA OR ABUSE
- SELF ESTEEM
- PERSONALITY
- INTRA-PERSONAL CONFLICTS

RELATIONAL & SOCIAL

- INTER-PERSONAL CONFLICTS
- SEXUAL DYSFUNCTION IN PARTNER
- MIS-COMMUNICATIONS
- FAMILY & FINANTIAL PROBLEMS

modified from Basson et al, 2004

International Menopause Society
promoting education and research on all aspects of adult women's health
www.imsociety.org

STRATEGIES TO MAINTAIN SEXUALITY IN MENOPAUSE

General education	• Awareness • Permission to discuss • Basic counselling
Recognition of signs and symptoms	• Being proactive • Pelvic examination to identify VVA • Interviews/questionnaires for HSDD
Promotion of health	• Lifestyle recommendations • Prevention of diseases
Attention to the partner	• General and sexual health • Feelings and quality of relationship
Individualization of treatment	• Hormonal strategies • Non-hormonal compounds • Psychosocial intervention

Nappi et al, 2014

BASIC SEXUAL COUNSELLING

- Give the woman opportunity to talk about her own sexuality
- Listen actively
  - Patient feels accepted and understood
  - Emotional relief
- Inform about the reality of human sexuality
  - Put the variety of personal experiences into perspective
  - Frequency of problems
  - Differences between female and male sexuality
  - Knowledge
  - Empowerment
- Dispel myths about male and female sexuality

Giulia, 59 yrs
DYSPAREUNIA

CLINICAL CASE 1

- 5 years postmenopause
- Nulliparity
- Symptoms of VVA (dryness, urgency/frequency)
- Happy marriage of 18 years with a 53 yrs man
- Willing to be sexually active, for the past 2 years orgasmic difficulties and recurrent/ postcoital cystitis. Her sexual drive is still there.
- Mild climacteric syndrome (joint pain, fatigue, anxiety)
- Hypertension controlled by medications (betablockers)

Nappi et al, 2014

CLINICAL CASE 1

Giulia, 59 yrs
DYSPAREUNIA
What are your steps?

- Look for Signs of VVA
- Evaluate pelvic floor hypertonicity
- Use a bladder symptom screening tool
- Rule out urinary infections
- Pharmacological history (anxiolytics, diuretics)
- Check androgens, thyroid, prolactin, other markers of CVD risk
- Be sure she exercises regularly
- Get information on intra-personal (body image, regret infertility) and inter-personal factors (partner's health, commitment, role)

Nappi et al, 2014

CLINICAL CASE 1

Giulia, 59 yrs

DYSPAREUNIA

What are your therapeutic choices?

- Lubricants to avoid friction during intercourse and other non-hormonal strategies (moisturizers, supplements,…) with a positive effect on vaginal mucosa
- Local ET, because signs of VVA are there
- SERM such as ospemifene, if no contraindicated
- Pelvic floor exercises and other physical therapies (self-massage, genital awareness) to avoid hypertonicity and improve vascularization
- Drugs for overactive bladder (OAB)
- Change the antihypertensive drug
- Life-style modifications
- Sexual counselling for the couple

Nappi et al, 2014

Teresa, 54 yrs
LOW DESIRE
(HSDD)

CLINICAL CASE 2

- 3 years post menopause
- 2 vaginal deliveries
- Gradual reduction of sexual desire and interest for the past 4 years
- Marriage of 22 years with few conflicts
- When sexually active, she is very rarely aroused from physical stimulation, genital or non-genital. Her last orgasms were some 3 years ago
- History of postpartum depression
- Diet and exercise for glucose intolerance

Nappi et al, 2014

Teresa, 54 yrs
LOW DESIRE
(HSDD)
What are your steps?

CLINICAL CASE 2

- Obstetric History/Pelvic floor dysfunction
- Look for Signs of VVA
- Rule out vaginal candidiasis
- Assess climacteric syndrome (mood disorders)
- Use a questionnaire to assess sexual distress
- Check androgens, thyroid, prolactin, glucose
- Pharmacological history (antidepressants)
- Get information on intra-personal (body image, self-esteem) and inter-personal factors (partner's general/sexual health, communications, discrepancies in desire for sex, social role)

Nappi et al, 2014

CLINICAL CASE 2

Teresa, 54 yrs
LOW DESIRE
(HSDD)
Is she a candidate to hormonal treatments?

- Yes, systemic MHT (EP/Tibolone) if she has climacteric syndrome and the risk/benefits profile is favorable
- Yes, local ET if signs of VVA are there
- Yes, Testosterone may be used, but only if distress is documented
- Maybe, before we need to rule out any other potential contributors (depression, thyroid problems, urinary incontinence, infections, drug use,…)
- No, before it is better to have the partner checked for medical conditions/sexual dysfunction
- No, the first-line treatment should be always psychosexual therapy and cognitive reconstruction

Nappi et al, 2014

Carla, 52 yrs
VVA, BREAST CANCER

CLINICAL CASE 3

- Chemotherapy induced menopause 3 years ago
- 1 kid delivered by cesarean section (elective)
- Symptoms of VVA (dryness, dyspareunia, burning)
- Marriage "on the rocks" after 25 yrs
- No sexual activity for the past 2 years, but sexual intercourses have been painful even before.
- Severe climacteric syndrome (hot-flushes, depression, insomnia, poor memory, joint pain, fatigue, anxiety)
- Hypothyroidism controlled by L-thyroxine
- Smoker (more than 10)

Nappi et al, 2014

Carla, 52 yrs
VVA, BREAST CANCER
What are your steps?

CLINICAL CASE 3

- Check if she is on endocrine chemotherapy
- Look for Signs of VVA including vaginal vault size
- Obstetric History/Pelvic floor dysfunction
- Rule out a real psychiatric diagnosis (major depression)
- Assess the presence of other comorbidities
- Check androgens, thyroid, prolactin
- Get information on previous satisfaction with body image/sexuality/quality of the relationship, actual self-esteem, coping abilities, couple/family dynamics, support network, social role)

Nappi et al, 2014

CLINICAL CASE 3

Carla, 52 yrs
VVA, BREAST CANCER
What are your therapeutic choices?

- Smoking cessation and other life-style modification (not using scented soaps, panty liners,…)
- SSRIs to relieve some symptoms (hot-flushes, depression)
- Change to an alternative anti-estrogen, if possible
- Pelvic floor exercises and other physical therapies (self-massage, genital awareness, body image improvement)
- Discuss with the patient and the oncologist the risk and benefits of local ET
- May use estriol and testosterone preparations, after appropriate counselling
- Psycho-sexual counselling for the couple

Nappi et al, 2014

Laura, 62 yrs
NO SEXUAL ACTIVITY

CLINICAL CASE 4

- 13 years postmenopause
- 2 vaginal deliveries
- Widowed for 5 years
- Not sexually active, but she is reconsidering sex because of a new partner (67 years in good health)
- Recurrent urinary infections (UTIs) for the past 2 years and occasionally vulvo-vaginal dryness/burning; a recent episode of light bleeding
- Severe osteopenia treated with Vitamin D/Calcium
- Benzodiazepines when needed
- No other medical conditions

Nappi et al, 2014

CLINICAL CASE 4

Laura, 62 yrs
NO SEXUAL ACTIVITY
What are your steps?

- Look for Signs of VVA, including vaginal vault size, low elasticity, fissures, alkaline pH
- Evaluate pelvic floor function
- Rule out urinary infections
- Ask for pelvic ultrasound, mammography and BMD density
- Check androgens, thyroid, glucose, other markers of CVD risk
- Assess her mental health
- Get information on intra-personal (body image, feeling guilty, shame) and inter-personal factors (partner's sexual health, communications, family/financial problems)

Nappi et al, 2014

CLINICAL CASE 4

Laura, 62 yrs
NO SEXUAL ACTIVITY

What are your therapeutic choices?

- Lubricants to avoid friction during intercourse and other non-hormonal strategies (moisturizers, supplements,…) with a positive effect on vaginal mucosa and bladder function
- Local ET, because signs of VVA are there
- SERM such as ospemifene
- Systemic MHT because of severe osteopenia and VVA
- Pelvic floor exercises and other physical therapies (self-massage, genital awareness) to improve muscle function and vascularization
- PDE5-inhibitors/other blood vessel dilators
- Individual psychotherapy

Nappi et al, 2014

CASO CLINICO

Giovanna, 48 anni

Profilo della donna

- UM: luglio 2013 (precedente aprile)
- Da 1 anno ipomenorrea/oligomenorrea
- Coniugata, 2 PVN
- Impiegata in uno studio legale
- EP dai 20 ai 30 anni, sospesa x cefalea
- BMI: 23.2 kg/m^2
- Fumo: 5/die; caffe':4/die; alcool: sociale
- Alimentazione: varia e regolare; Attività fisica: piscina 1 v/sett
- Genitori viventi: madre ipertensione arteriosa, depressione maggiore; padre k colon

Profilo sintomatologico e clinico

- Vampate e sudorazioni diurne/notturne
- Cefalea tensiva (almeno 3-4 gg a sett)
- Irritabilità, ansietà, risvegli notturni
- Frequenza urinaria, 3 episodi di cistite nell'ultimo anno
- Dispareunia/Bruciore dopo il rapporto
- Riscontro occasionale di PA diastolica > 80
- Aumento dei trigliceridi > 150 mg/dl; colesterolo HDL nella norma; omocisteina ai limiti superiori
- Modesto aumento di peso (2-3 kg)

CASO CLINICO

Susanna, 54 anni

Profilo della donna

- UM: marzo 2012
- Annessiectomia dx 2001 x cisti endometriosica
- Separata, mai gravidanze
- Direttrice di filiale di banca
- EP dai 42 ai 52 anni
- BMI: 21.7 kg/m^2
- Fumo: ex (15 anni fa); caffe':1/die; astemia
- Alimentazione: sana e variata; Attività fisica: pilates 2 v/sett
- Genitori deceduti: madre Parkinson esordito a 66 anni; padre k polmone

Profilo sintomatologico e clinico

- Vampate e sudorazioni diurne (già fitoestrogeni senza beneficio)
- Tachicardia postprandiale
- Insonnia dai 40 anni (benzodiazepine al dormire)
- Deficit di memoria, senso di confusione, perdita di assertività e del senso di autonomia
- Artralgie/mialgie diffuse/secchezza cutanea
- Rapporti sporadici dolorosi/Scarso desiderio/deficit orgasmico
- MOC lombare T-score -2.4
- Valori di TSH ai limiti inferiori

CASO CLINICO

Luisa, 52 anni

Profilo della donna

- UM: febbraio 2013 (precedente dicembre)
- Dal 2010, terapia progestinica x flussi menometrorragici
- Coniugata, 1 POV
- Ha una tabaccheria
- IUD dal 2006 al 2010, mai EP
- BMI: 28.4 kg/m^2
- Fumo: 10/die; caffe':2/die; alcool: vino ai pasti
- Alimentazione: tendenza alle abbuffate notturne; Attività fisica: porta a spasso il cane
- Genitori viventi: madre diabetica, ipertesa; padre IMA

Profilo sintomatologico e clinico

- Scarsa sintomatologia vasomotoria
- Lieve depressione
- Algie pelviche/senso di gonfiore
- Incontinenza da stress (peggiorata nell'ultimo anno)
- Deficit di lubrificazione, spesso leucorrea
- Ipertesa in terapia con betabloccante/diuretico
- Aumento dei trigliceridi > 150 mg/dl; colesterolo LDL 195 mg/dl; glicemia 121 mg/dl
- Ulteriore aumento di peso (8 kg) nell'ultimo anno con distribuzione androide del grasso corporeo

CASO CLINICO

Maria Stella, 41 anni

Profilo della donna

- UM: marzo 2013 (precedente gennaio da EP sospesa per desiderio di maternità)
- Convivente, IVG 19 anni
- Commessa
- EP per lunghi periodi, sospesa ciclicamente per spotting/ipomenorrea
- BMI: 22.1 kg/m^2
- Fumo: mai; caffe': d'orzo; alcool: vino a cena
- Alimentazione: disordinata; Attività fisica: ha interrotto x tendinite
- Genitori viventi: madre k mammella, osteoporosi; padre cirrosi epatica

Profilo sintomatologico e clinico

- Più di 15 vampate/sudorazioni diurne
- Insonnia, ansia libera, distimia
- Un accesso in PS per tachicardia/fame d'aria/rialzo pressorio (attacco di panico, benzodiazepine al bisogno)
- Artralgie localizzate alle mani e ai piedi/Affaticamento
- Dispareunia introitale/deficit di lubrificazione/calo notevole della libido
- TSH ai limiti superiori, Colesterolo tot 245 mg/dl; HDL 67 mg/dl; trigliceridi 144 mg/dl
- Aumento repentino di peso (circa 4 kg) e gonfiore agli arti inferiori