

Effects of menopause and hormone replacement therapy (HRT) on quality of life of women

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Most natural menopause occurs in elderly women (48-52), so there are confused manifestations of aging.

Early menopause due to premature ovarian failure

- Before the age of 40 years
- May be due to ovarian resection, chemotherapy, radiation therapy: sudden
- Or due to low oocyte reserve, for example Turner syndrome 45, XO ...

causes much disturbance and more reduction of quality of life.

Sexual hormones stimulate the central nervous system to synthesize *endogenous opioids*:
Endorphins, Enkephalins, Dynorphins.

Sex hormones reduced so endorphins are not secreted, causing a large number of functional symptoms of menopause.

Estrogen and cardiovascular disease

- Young women seem to be protected from cardiovascular disease
- Menopause and old age are high risk factors for cardiovascular disease.
- Each organ contains stem cells, which help the body to repair its own lesions, such as fractures and soft part wounds...

Doris A. Taylor et al. Texas Heart Institute at St. Luke's Episcopal Hospital, Houston, TX, reported at the NAMS Dallas conference 9 – 12 Oct 2013

Estrogen and cardiovascular disease

- **CD34** is the stem cell that circulates in the blood, in the presence of **Estrogens**.
- **Tuổi già:** decreased CD34, increased inflammatory cytokines, increased monocytes.
- **CD34 protects blood vessels:** Injection of CD34 into atherosclerotic blood vessels of rats showed decreased embolism, decreased apoptosis, decreased inflammatory cytokines, increased vascular endothelial growth factor (VEGF)

Doris A. Taylor et al. Texas Heart Institute at St. Luke's Episcopal Hospital, Houston, TX, reported at the NAMS Dallas conference 9 – 12 Oct 2013

Level I prophylaxis for cardiovascular disease by hormone replacement therapy

| Results | <i>Hormone replacement therapy</i> ^{1,2*} | Lipid lowering drugs ³ | Aspirin ⁴ |
|-------------------------------|--|--|----------------------|
| Cardiovascular disease | 0.68 (0.48-0.96) | 0.89 (0.69-1.09) | 0.91 (0.80-1.03) |
| Overall death | 0.61 (0.39-0.95) | 0.95 (0.62-1.46) | 0.95 (0.85-1.06) |

* Women < 60 years of age and/or <10 years after menopause when started to use one of three drugs (divided into 3 randomized groups)

¹Salpeter S, et al. *J Gen Intern Med* 2004;19:791-804.

²Salpeter S, et al. *J Gen Intern Med* 2006;21:363-366.

³Walsh JME, et al. *JAMA* 2004;21:363-366.

⁴Ridker PM, et al. *N Engl J Med* 2005;352:1293-1304.

Osteoporosis and menopause

Prophylaxis of osteoporosis after menopause

- Adequate calcium dietary intake from adolescence
- **Taking estrogen - ovarian hormone replacement therapy when menopause**
- Doing exercise
- Avoiding risk factors

Alzheimer's disease

Cerebrovascular



1/3 of the brain volume is blood vessels, which will affect brain function if damaged

Menopause and brain



When menopause, ovaries stop working:

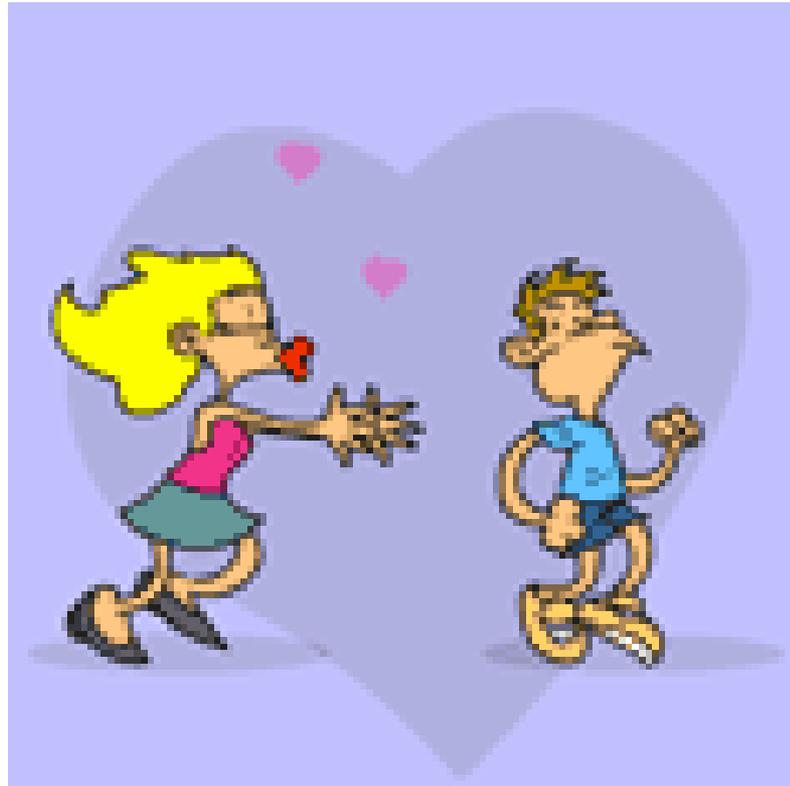
-  serum estrogen   brain energy
-  glucose metabolized in brain = step I of brain aging
-   ketone in brain, leading to dysfunction of mitochondria,
-  brain activity.
- **Surgical resection of two ovaries causing early E2 reduction which will increase the rate of Alzheimer's disease to 70%.** If using E2 after surgery, the rate of the disease is normal.

*Pauline M. Maki, Univers Illinois – Chicago
(reported at the NAMS-Dallas 2013 conference)*

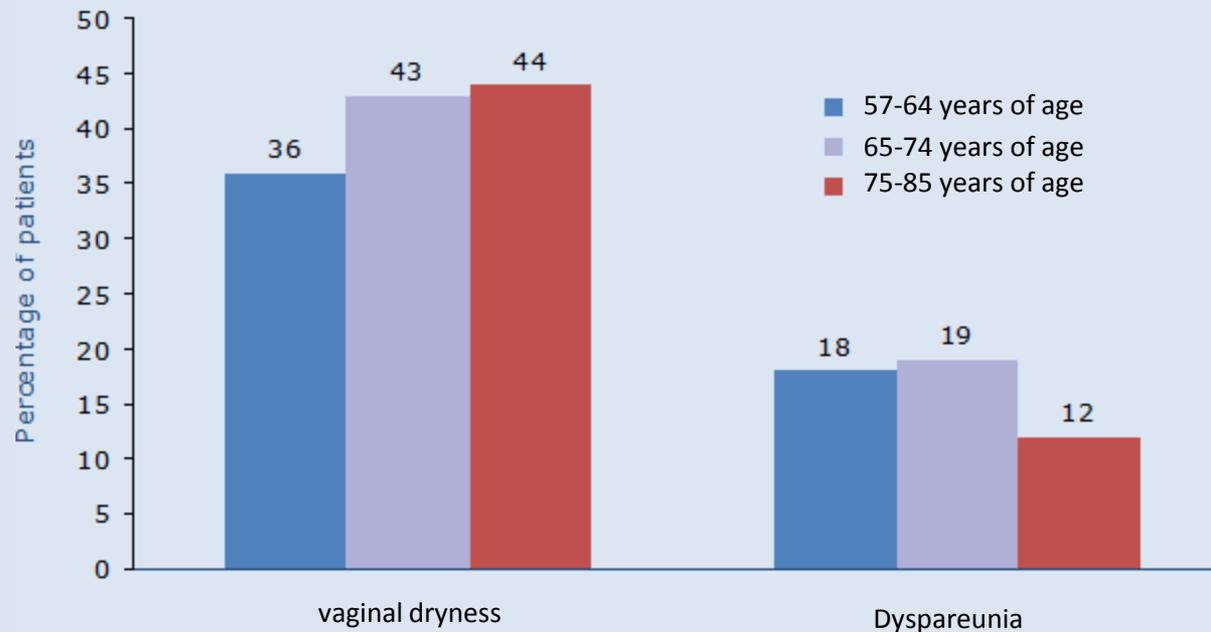
Can the brain be trained and recovered?

- ✿ The frontal lobe of brain and connective bonds are the ultimate developmental sites, until the age of 20 years fully completed, but they are the first degeneration sites, about the the mid age of 40 years.
- ✿ In order to prolong the life of brain, **regular and continuous intellectual work, exercise may be good measures to protect brain**, they slow down dementia, reduce the burden of amyloidosis, strengthen the connection in the frontal lobe and the hippocampus.
- ✿ **The production of new neurones as well as new transmission nerves between new neurones** in the ages of 40-50 years has been demonstrated.

Urogenital dysfunction in women

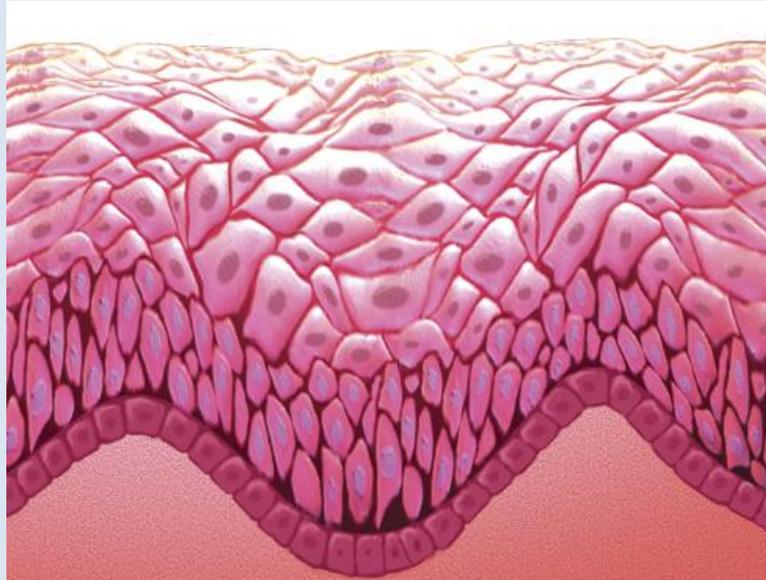


About one-third of women over 56 years of age avoid sexual intercourse because of related issues¹

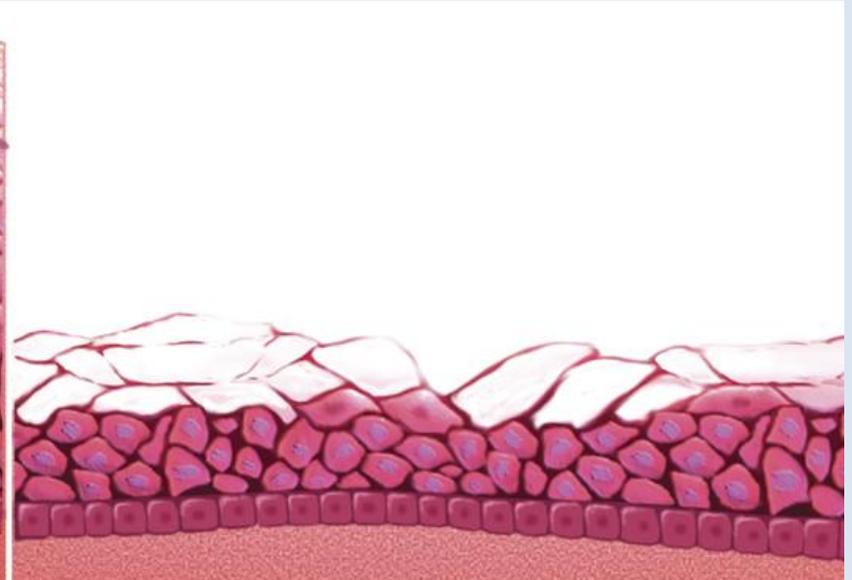


1. Lindau ST et al. *N Engl J Med* 2007; 357: 762–774

VAGINAL ATROPHY: Vagina and cell structure changes



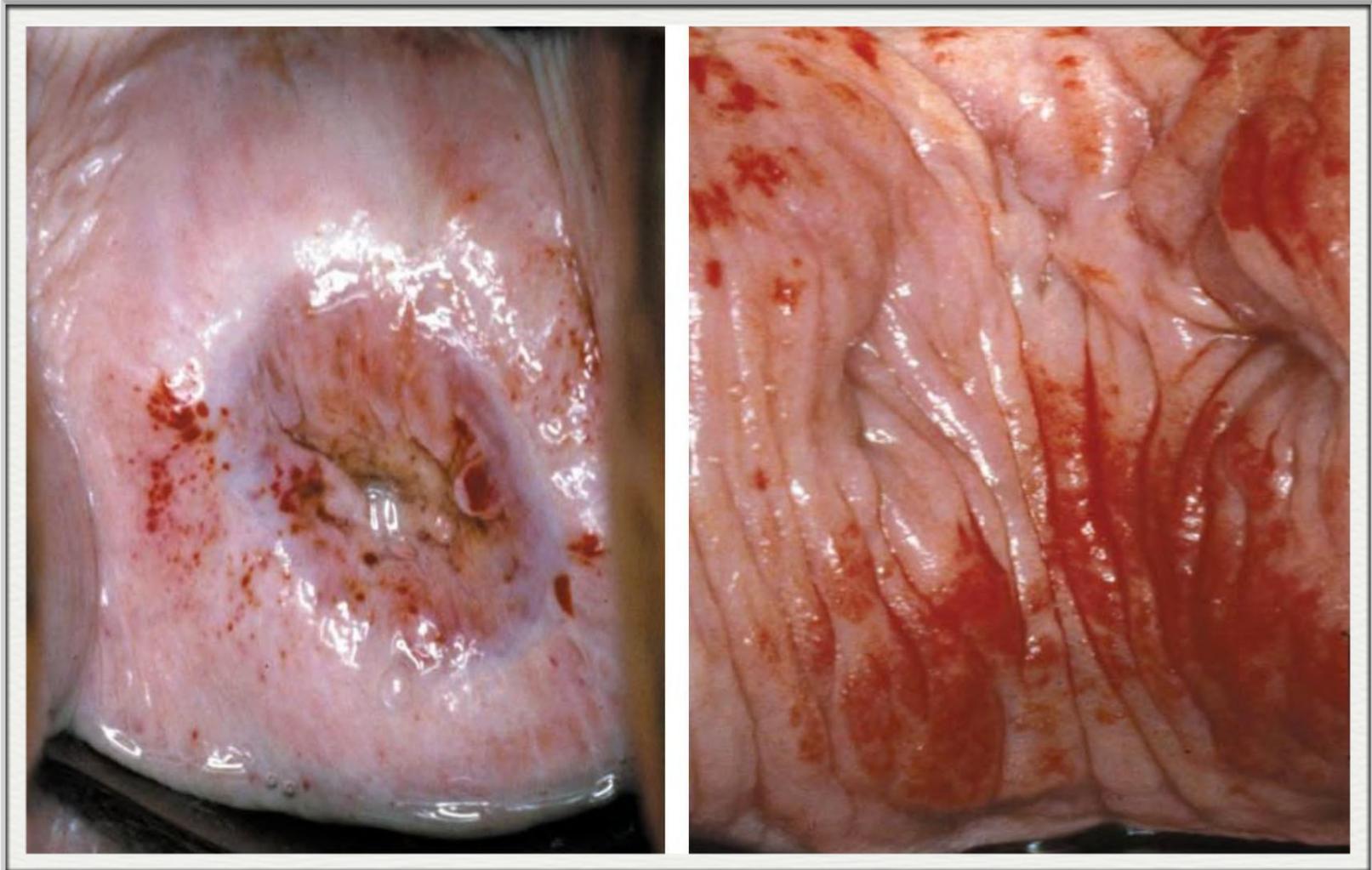
Thick, healthy, full estrogen vaginal surface



Thin, dry vaginal surface due to menopause (after estrogen loss)



- Menopausal women naturally after 2 years
- No estrogen replacement therapy
- Loss of lip and vulva thickness
- Urethra and vaginal mucosa paleness
- Decreased vaginal humidity

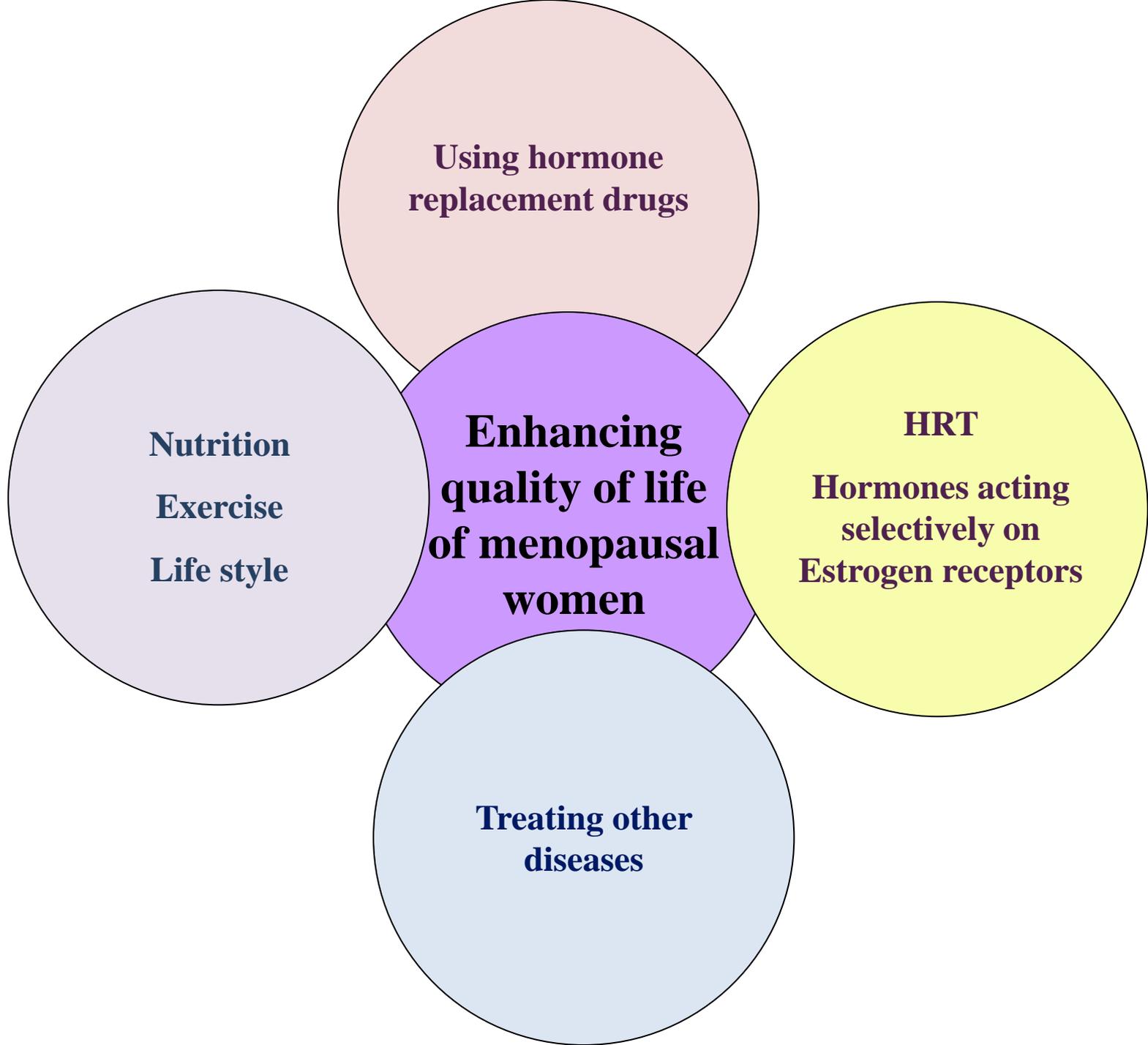


Apgar, Brotzman, Spitzer

Summary

Menopause can have negative effects on quality of life of women

1. Many of functional symptoms causing fatigue and discomfort, although they only occur in perimenopause within a short time. These symptoms can be easily treated with hormone replacement therapy.
2. Menopause can increase incidence of cardiovascular disease.
3. Menopause increase rate of osteoporosis.
4. Post-menopause women may have dementia.
5. Urogenital-sexual dysfunction (genitourinary syndrome of menopause, GSM) is also a problem of the age of menopause.
6. In addition, due to age, women may have many other diseases such as female genital cancers that we do not mention in this report.



Using hormone replacement drugs

HRT
Hormones acting selectively on Estrogen receptors

Treating other diseases

Nutrition
Exercise
Life style

Enhancing quality of life of menopausal women

HORMONE THERAPY

IMS 2016 Recommendation on menopausal hormone replacement therapy - General Principles of hormone use

- Hormone replacement therapy (HRT) is still **the most effective therapy** for vasomotor symptoms and other functional symptoms.
- Using the lowest effective dose of estrogen
- Adjusting the dose according to each patient
- **Using as long as benefits are still higher than risks**
- Benefit/risk balance
 - It is more favourable if starting early treatment during menopause period
 - Risk/benefit re-evaluation.

Treatment opportunity window

- ▶ Menopausal women, 50-59 years of age, or under 60 years of age,
- ▶ New menopause less than 10 years, preferably less than 6 years
- ▶ Women over the age of 60: risk is higher than benefit



Contraindications

- ▶ **History of or currently having breast cancer**
- ▶ **Had manifestation of cardiovascular disease**
- ▶ **History of venous thromboembolism (or pulmonary embolism)**
- ▶ **Acute liver failure, acute kidney failure**
- ▶ **Unexplained abnormal vaginal bleeding.**
- ▶ **Oral Estrogen: Relative contraindication in women with high serum triglycerides, biliary tract disease, with abnormal Factor V Leiden although there was no manifestation of arteriovenous thromboembolism.**
- ▶ **Patients with migraine headaches: contraindications for oral estrogen use, only transdermal use.**

Choosing Estrogen in hormone replacement therapy

There are many types of Estrogen used in HRT such as :

- conjugated equine estrogens (CEE),
 - ethinyl estradiol (EE) ,
 - 17β -estradiol.

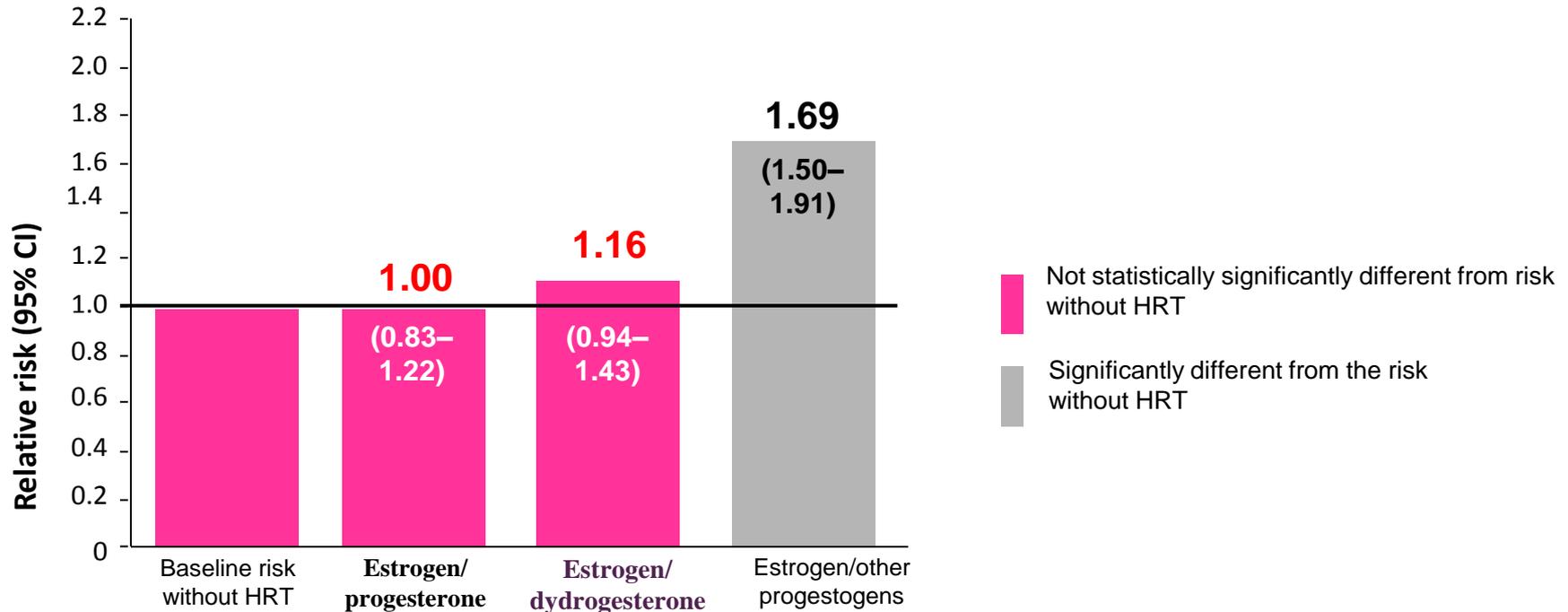
Which type of Estrogen should be chosen?

Choosing Estrogen in hormone replacement therapy

- **17 β -estradiol** is an estrogen synthesized by ovarian follicle granulosa cells.
- Ethinyl estradiol is a synthetic estrogen, which is ten times stronger than 17 β -estradiol.
- Use of 17 β -estradiol will have less side effects, such as venous thromboembolism.

Progestogen choice and risk of breast cancer: E3N French cohort study

Risk of breast cancer

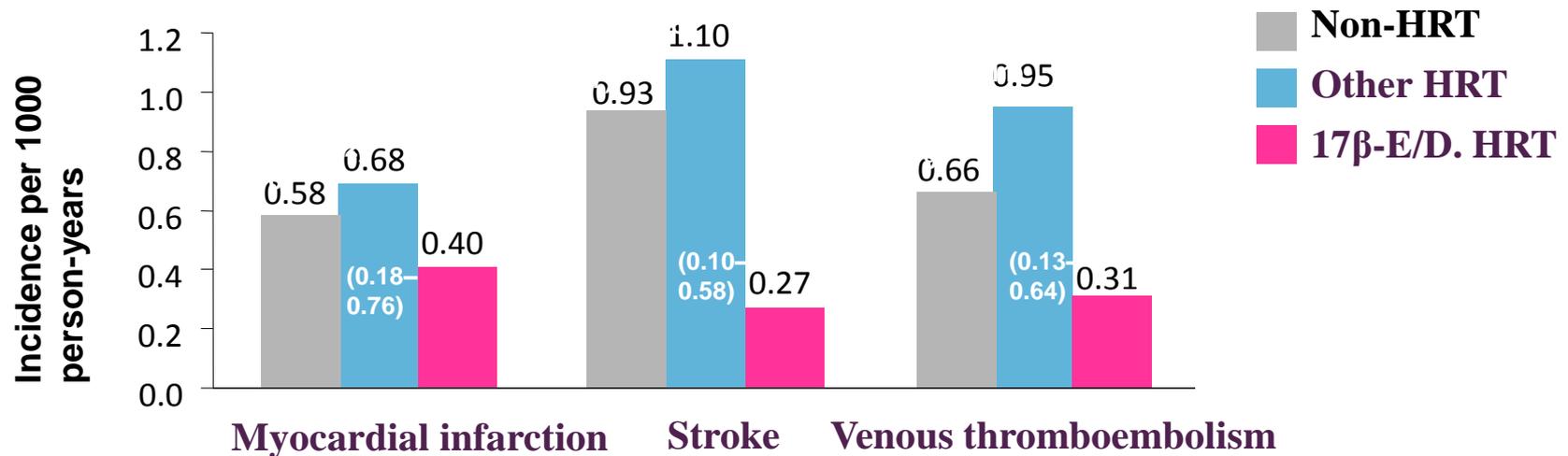


N = 80,377 women, for an average treatment duration of 8.1 years

Fournier A et al. Breast Cancer Res Treat 2008;107:103–11;
Fournier A et al. J Clin Oncol. 2008 ;26:1260–1268.

Estradiol/Dydrogesterone tends to reduce risk of cardiovascular disease

- Analysis of case-control studies based on UK-based General Practice Research Data (n = 69,412)
- 6 years follow up
- Using E/D many months to many years did not increase risk of cardiovascular events vs. using non-HRT or other HRT type



- Schneider C et al. Climacteric 2009;12:445–53.

IMS 2016 RECOMMENDATIONS

Encouraging patients to **actively tell** their **vulvovaginal atrophy-dryness (GSM)** symptoms and go to appropriate treatment facility [A]

Early treatment is best and should continue to maintain benefits

Treatment guidelines include urogenital physiology recovery and symptom relief

If GSM is the only symptom, **topical estrogen therapy** should be applied [B]

Key points

- **Topical estrogen therapy maximally limits systemic absorption and serum estradiol levels do not exceed normal limits (< 20 pg/ml) for postmenopausal women [B]**
- No need to supplement progestogen [B]
- Data on the use of topical estrogen in hormone-dependent cancer women is limited [D]

IMS recommendations. Climacteric 2016;19:109-50

OSPEMIPHENE

Selective Estrogen Receptor Modulator - (SERM)

Only effect at vagina

Improved (+) for 12 weeks
Improved VMI, vaginal pH, the most uncomfortable vaginal dryness symptom

2% reported hot flush

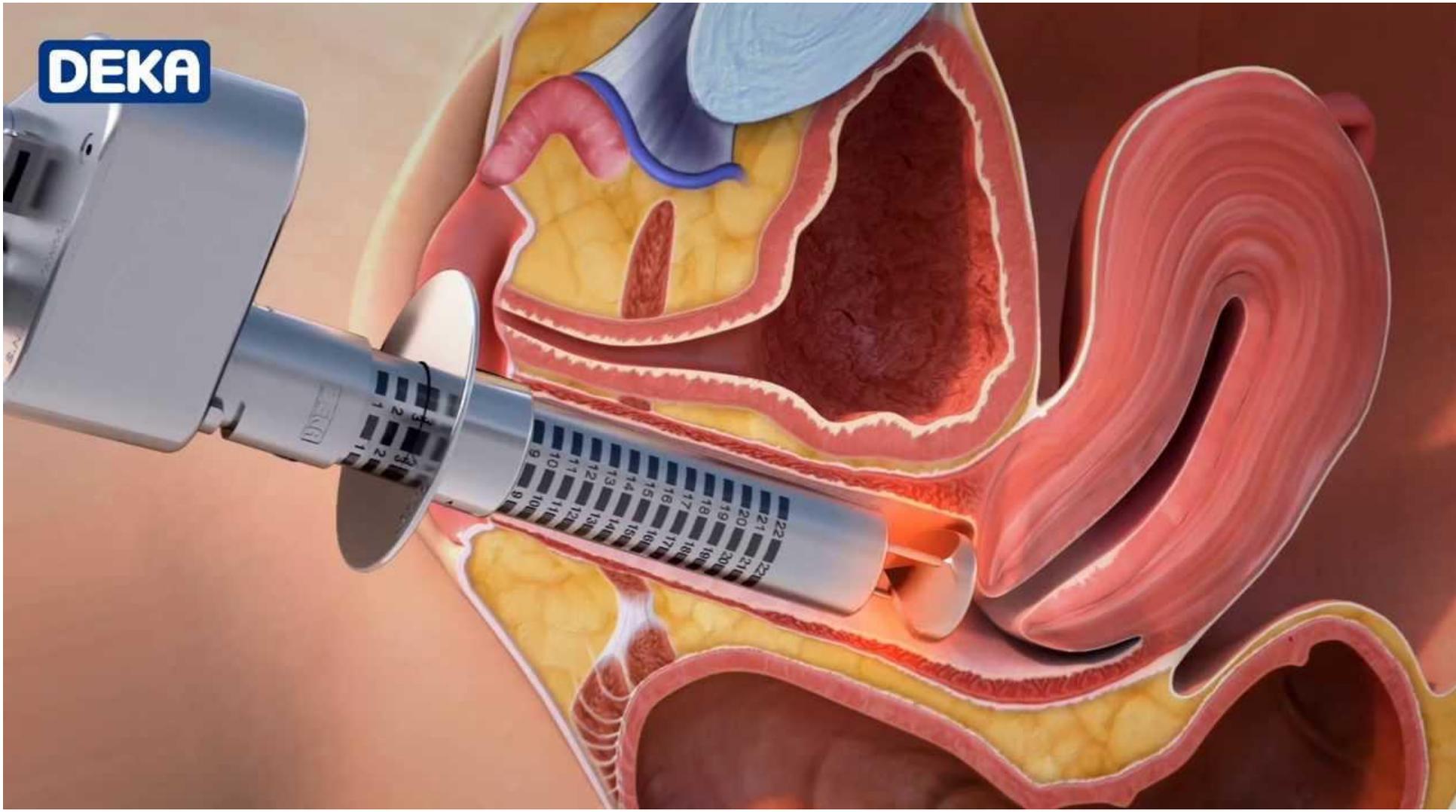
LASER THERAPY

VAGINAL REJUVENATION

Microablative fractional CO2 laser technology has the effect of “stimulating rearrangement of tissue structure”

- Activation of fibroblasts producing collagen and
- Stimulating endothelial growth factor for neo-angiogenesis with specific effects on epithelium

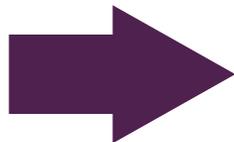
DEKA



NON-HORMONE THERAPY

NON-HORMONE THERAPY

- ▶ WHI published in 2002 caused great psychological concern
- ▶ Rate of decline in MHT use, serious decline occurred in developed countries
- **Germany: 40.2%** reduction in 2003 - 2004 compared to 1997 - 1999 (Du et al - BMC Women's Health 2007).
- **Australia: 55%** reduction in women 50-80 years of age in 2003 compared to 2001 (Travers et al., Australasia, N. Z. J of Obstet Gynaecol, 2006).
- **US: 77%** reduction in new MHT use in women 50-79 years of age in 2004 compared to 2001 (Weglenka et al., Women's Health 2006).



INTRODUCTION OF NON-HORMONE DRUGS

Isoflavones extracted from soy bean

Isoflavones in soy beans are often referred to as **herbal estrogen - phytoestrogen** because **isoflavones bind to both estrogen receptors, though it is weak.**

A pooled analysis of 13 studies with 602 women used # 6 - 12 months isoflavones and 594 placebo, showed a reduction in **menopausal symptoms** (mean reduction of **-20.62 with 95% CI (-28.38) - (-12.86)**).

Mechanism of action:

- genistein and daidzein aglycone from isoflavones are absorbed through intestine
- *Daidzein is converted by a type of enterobacteria into 2 types of equol: R(+) equol and S(-)-equol are the same as estrogen but rate of binding to globulin is less (45 – 50%).*
- *The bioavailability of isoflavones depends on whether the intestinal tract with enterobacteria produce S(-)equol or not.*

- ▶ Isoflavones and metabolites *effectively alleviate menopausal symptoms.*
- ▶ Isoflavones do not cause endometrial thickening, acting is only *1 part of million of estradiol on endometrium.*
- ▶ Isoflavones do not change breast tissue cells.
- ▶ An appropriate study is required, at least for 24 months, to see the effect of isoflavones on bone.

- ▶ *Soy bean isoflavones* can be used with *a starting dose of 50 mg or more daily, continuously for 12 weeks.*
- ▶ It is possible to give orally *3 g of soy bean sprout powder daily* to have enough of the above dose.
- ▶ It is needed *to continuously monitor* to detect undesirable effects
- ▶ *If after 12 weeks but the symptoms did not decrease, it must be changed to other treatment.*

Non-hormone therapy

- ▶ **Vitamin E 800 mg/day** can reduce a hot flush every day.
- ▶ **Omega 3**: contains unsaturated fats. Studies have shown that **omega-3 reduced menopausal symptoms more significantly** than placebo.
- ▶ **Herbal extract**:
 - Black cohosh, Crinum, Dioscorea, Gingseng: little effect

- **Maca – *Lepidium Meyenii* (Angela)**

This is a herb, commonly known as Peruvian Ginseng, has effect of increasing **strength, endurance and helping the body to adapt to external environment. It is used by people to treat anemia, infertility and used for sport athletes and for patients with decreased sexual activity.**

- *Maca – Lepidium Meyenii* (Angela)

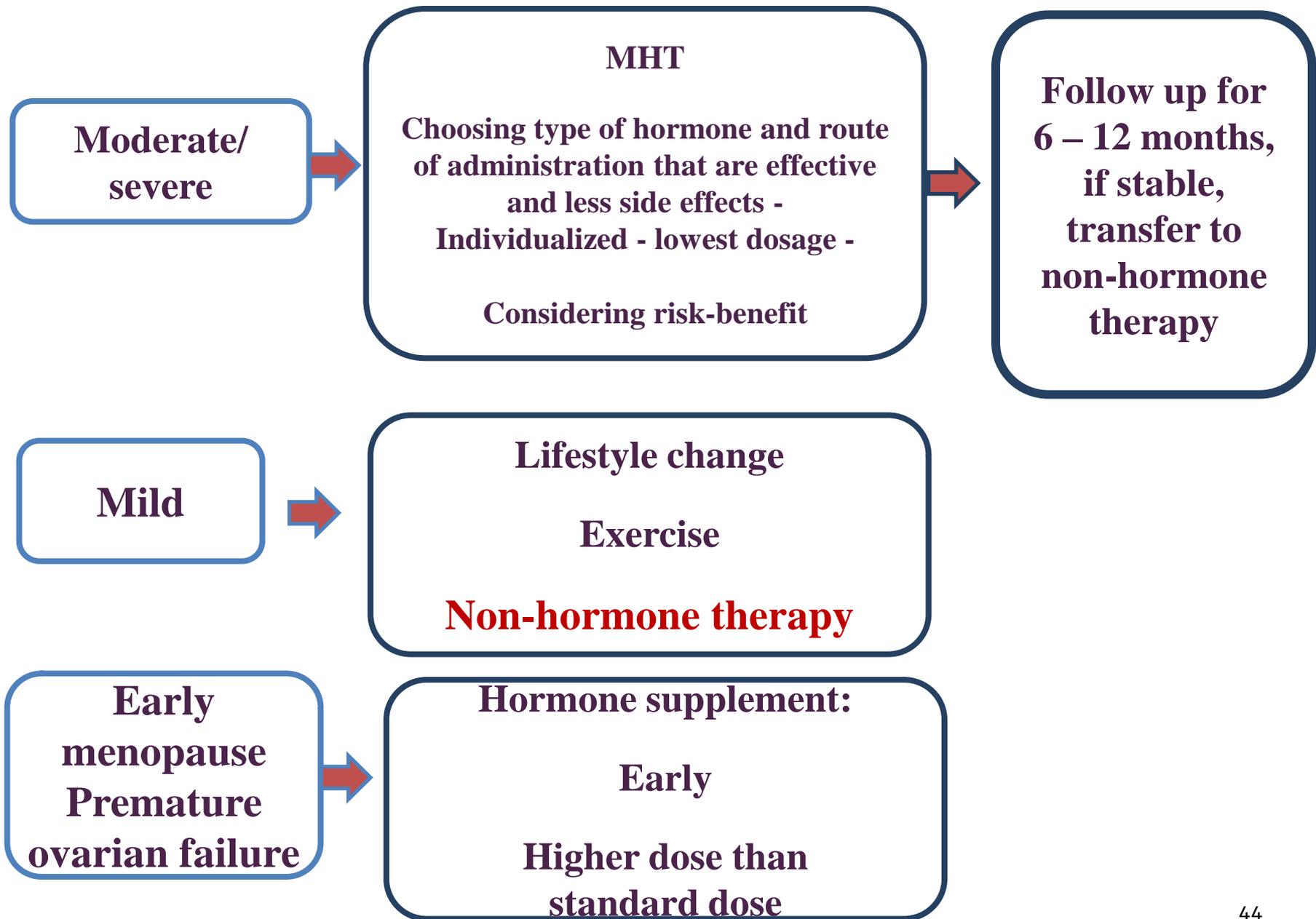
It has been studied abroad and in Vietnam and recognized that **having effect to regulate receptors of male and female sex hormones**. *Lepidium Meyenii* extracts contain estrogen, which may have a hormone supplement effect for women at the age of menopause.

Four studies of *Lepidium Meyenii* were analyzed and showed that the use of *Lepidium Meyenii* improved the Greene Climacteric index and the Kupperman index of quality of life.

Management of menopausal patients

▶ Treatment consideration:

- Determination: importance and impact level on quality of life, risk when treatment with hormone replacement therapy, full explanation of benefits and side effects; advice on lifestyle change, nutrition, exercise, non-hormone therapy
- Treatment decision is based on effect extent of symptoms





SINCERELY THANKS