HRT: Estrogens

Since many problems associated with the menopause are believed to be due to reduced estrogen levels, the main component of hormone replacement therapy (HRT) is estrogen.

The estrogens used in HRT are referred to as "natural" because they resemble substances produced in the body and include oestradiol, oestrone and oestriol which are usually made from soya beans or yam extracts. Conjugated equine estrogens made from horse urine are also sources of the naturally occurring estrogen oestrone sulphate.

If HRT is taken after a hysterectomy, usually estrogen alone is required. If HRT is taken when the womb (uterus) is still present, then estrogen is taken with a progestogen which prevents estrogenic stimulation and thickening of the womb lining. Estrogen can be taken by a daily tablet, twice weekly or weekly patch, weekly patch, daily gel or implant. People respond differently to different types, routes and doses of estrogen and sometimes several adjustments of therapy are required. If possible, any type should be tried for 3 months before deciding whether or not a change is required.

HRT: Progestogens

For women in whom the uterus (womb) is present, a progestogen is added to the estrogen to reduce the risk of estrogen causing thickening, and possibly cancer of the endometrium (lining of the womb). Progestogens are mostly made from plant sources and resemble the naturally occurring progesterone, usually produced from the ovary in the second half of the menstrual cycle. The two main types of progestogen currently used in HRT are: those most closely resembling progesterone (dydrogesterone, drospirenone medroxyprogesterone acetate and micronised progesterone) and those derived from testosterone (norethisterone, norgestrel and levonorgestrel).

If *side effects* are experienced on one type, changing the type or route of progestogen may help.

The *duration and frequency* of the progestogen determines the presence and pattern of bleeding and the type used is influenced by presence or absence of periods and age.

*HRT in the **Perimenopause**:* If HRT is commenced in the early stages of ovarian decline when periods are still present (the perimenopause),

estrogen is taken every day and progestogen for 10 to 14 days per month (*sequential HRT*). This cyclical progestogen induces a monthly withdrawal bleed in about 85% of women. If the periods are becoming infrequent, the progestogen can be taken for 2 weeks every 3 months, inducing a 3 monthly bleed (*long cycle HRT*).

*HRT in the **Postmenopause**:* If the periods have been stopped for more than 1 year (postmenopause) before starting HRT, or the women is aged 54 or more, progestogen can be taken every day along with the estrogen (*continuous combined HRT*). Continuous combined, or period-free HRT, may cause some bleeding in the first 6 months, but should not induce bleeding thereafter.

Mirena Coil.

This is a small device which fits inside the womb like an intrauterine conceptive device. It can usually be fitted in an out-patient clinic with minimal discomfort. Not only is it a contraceptive, but also it releases a small amount of progestogen hormone to the womb lining, making it thinner and hence making heavy periods lighter. At first it can sometimes be associated with irregular spot bleeding, which can be irritating, but this nearly always settles. Mirena can be used to provide the progestogen part of HRT in both the perimenopause and the postmenopause. With a Mirena in place, any form of estrogen can be used to control menopausal symptoms. Mirena is particularly helpful when there are heavy bleeds with sequential HRT, when contraception is still required along with HRT, and when there are side effects from the progestogen part of HRT

HRT: Route of HRT

If estrogen is only required for vaginal or urinary symptoms, vaginal estrogen is available in the form of a tablet, cream, or vaginal ring.

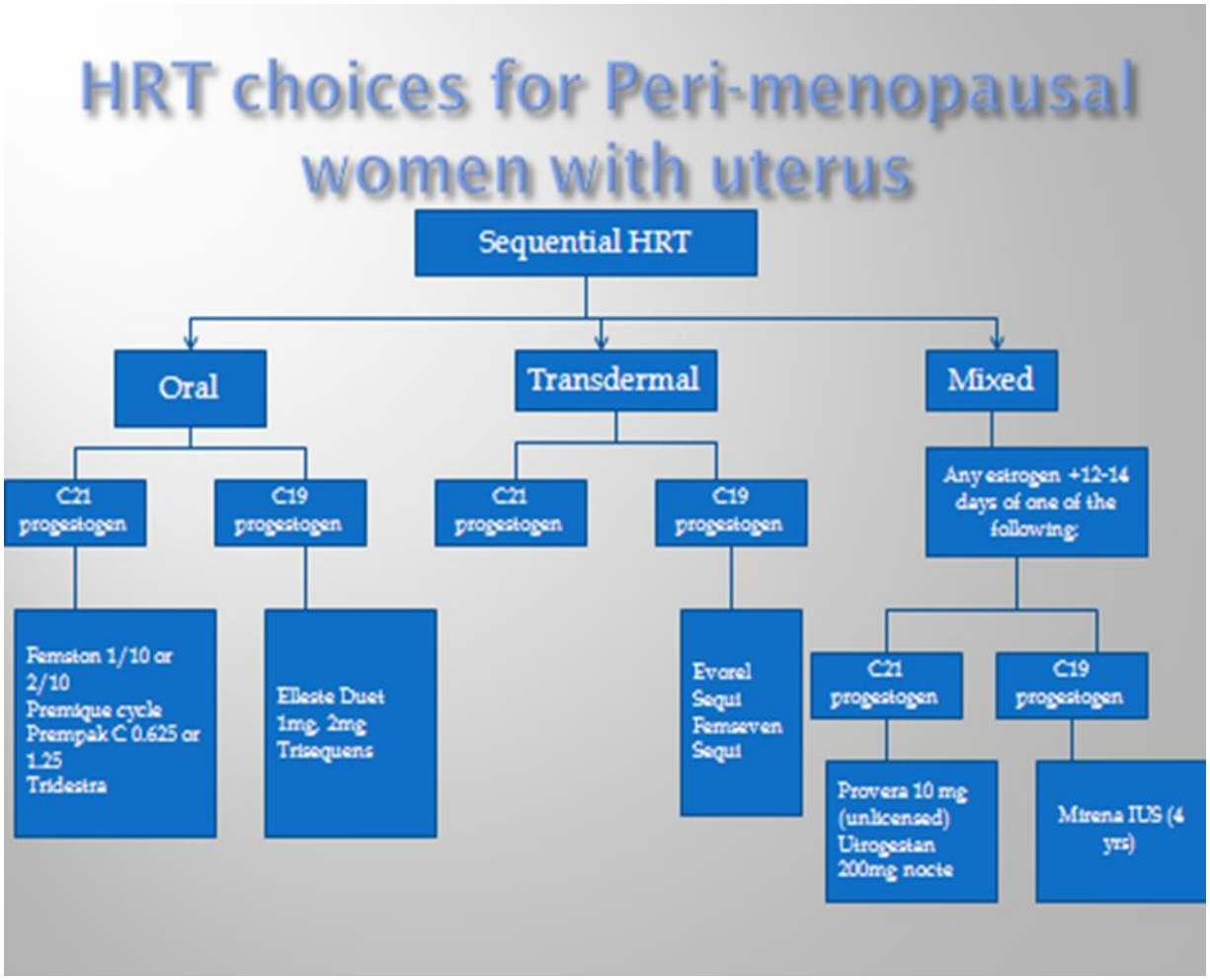
Vaginal oestrogens can be used indefinitely without the need to add back progestogens.

If estrogen is required for more general symptoms such as flushes, sweats, joint aches or poor sleep, then it is taken in a form which circulates throughout the body and is known as systemic HRT. Systemic estrogen can be taken as a daily tablet, a weekly or twice weekly patch, daily gel, or a 6 monthly implant. Estrogen combined with progestogen can be taken by tablet or weekly or twice weekly patch, and progestogen alone can be taken by tablet, vaginal gel or by the progestogen releasing intra-uterine system-Mirena. The different routes of estrogen used have

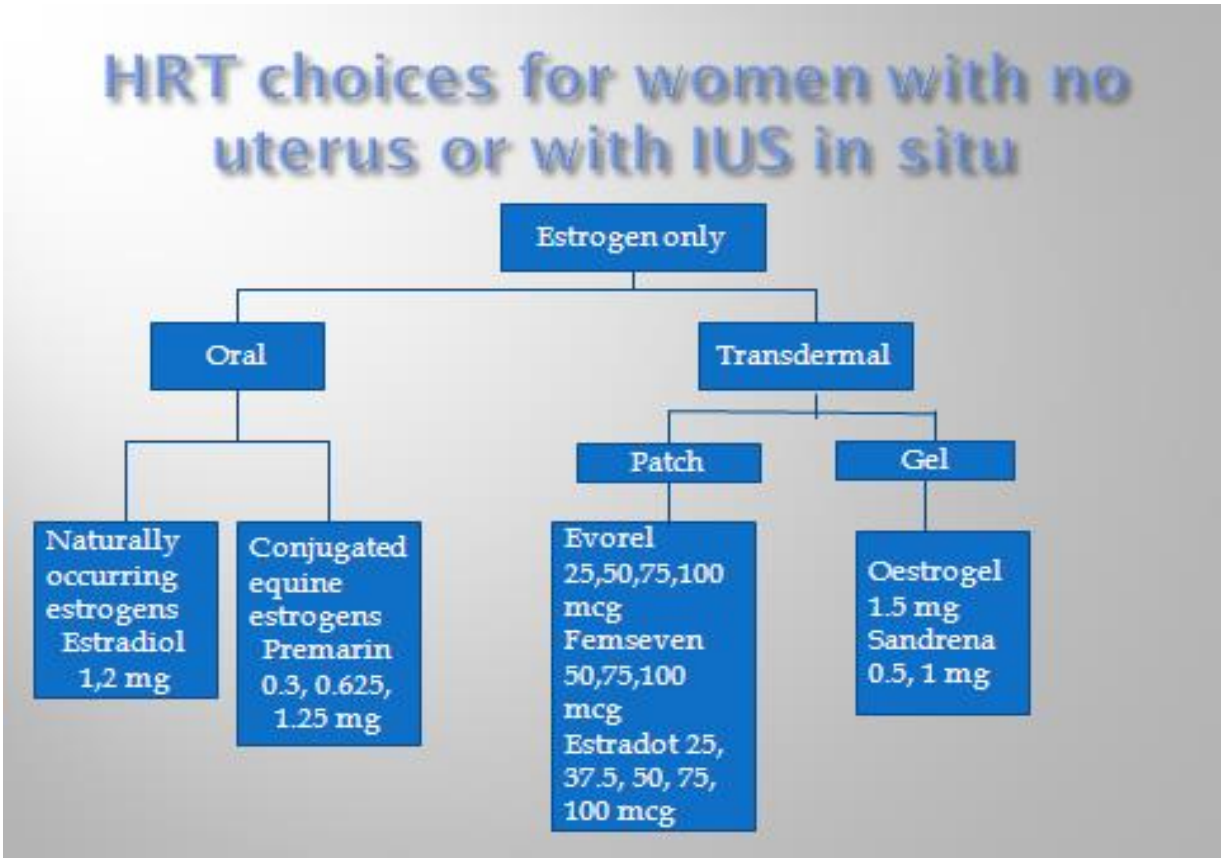
different metabolic effects (e.g. on clotting factors and blood fats) but the implications of the differences is controversial and the main factors determining choice of route are individual preference, response and past medical history. Most often, HRT is started in tablet form.

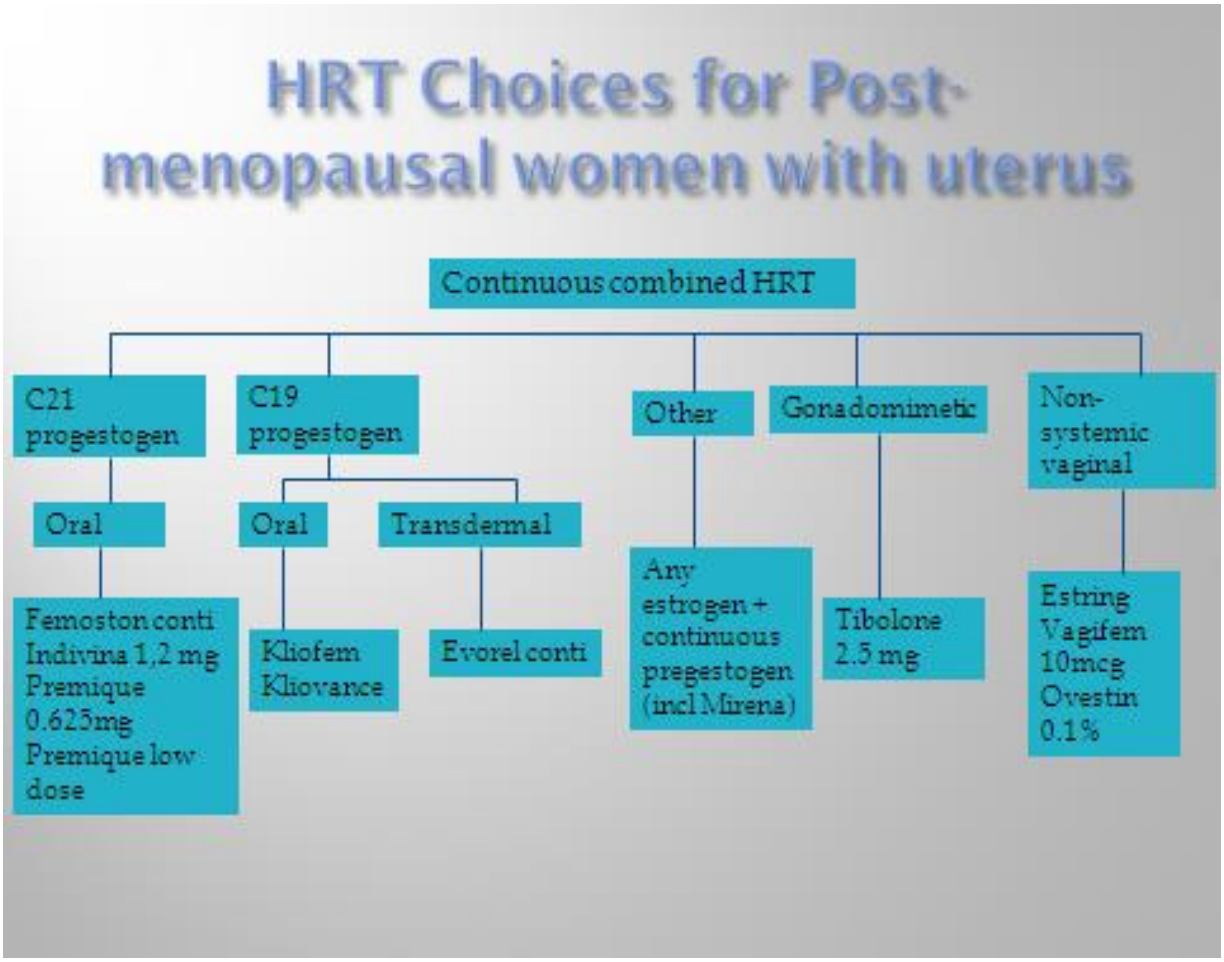
Indications for non-tablet route.

- Individual preference.
- Poor symptom control with tablet HRT.
- Side effects such as nausea with tablet.
- Bowel disorder which may affect absorption of tablet therapy.
- History of migraine (when steadier hormone levels which may be achieved with a patch may be beneficial).
- Lactose sensitivity (all tablet preparations of HRT contain lactose).
- History of gallstones.
- Current use of medications such as anti-epileptic medication which may interfere with the break-down of tablet HRT.
- Variable blood pressure.
- High triglyceride levels.
- Risk factors including Body Mass Index greater than 30, family history or past history of deep vein thrombosis or pulmonary embolus, after full discussion and specialist advice when necessary


HRT choices for Peri-menopausal women with uterus
Sequential HRT
Oral
Transdermal
Mixed
C21 progestogen
C19 progestogen
C21 progestogen
C19 progestogen
Any estrogen +12-14 days of one of the following:
Femoston 1/10 or 2/10
Premique cycle
Prempak C 0.625 or 1.25
Tridestra
Elleste Duet 1mg, 2mg
Trisequens
Evorel Sequi
Femseven Sequi
C21 progestogen
C19 progestogen
Provera 10 mg (unlicensed)
Utrogestan 200mg nocte
Mirena IUS (4 yrs)

* See N.B below


HRT choices for women with no uterus or with IUS in situ
Estrogen only
Oral
Transdermal
Patch
Gel
Naturally occurring estrogens Estradiol 1,2 mg
Conjugated equine estrogens Premarin 0.3, 0.625, 1.25 mg
Evorel 25,50,75,100 mcg
Femseven 50,75,100 mcg
Estradot 25, 37.5, 50, 75, 100 mcg
Oestrogel 1.5 mg
Sandrena 0.5, 1 mg



* NB the SPC for Mirena IUS from Bayer states that it can be used for 4 years for endometrial protection with HRT but the Faculty of Sexual and Reproductive Healthcare states that it can be used for 5 years in this situation FSRH Clinical Guidance on IUC June 2015 (unlicensed use).

The IUS Levosert is not licensed for endometrial protection.

Advice to women on stopping HRT – from the NICE Guidance 2015

- There were a variety of different methods of tapering and follow-up time of outcomes varied. Outcomes assessed were vasomotor, quality of life, return to HRT or use of alternatives.

- Women who have experienced a premature menopause should be told about the importance of taking hormonal treatment and continuing it to at least the age of expected menopause. Both HRT and COC are bone protective, HRT is not a contraceptive and HRT may improve blood pressure.

- It was considered that a woman's personal preference was most important.

- Women have previously been advised to stop HRT after 2-5 years of use or at the age of 60, but the NICE guidelines states that there is no certain evidence for this advice.

- In discussing continuation, the benefits and risks should be reviewed so that women can make an informed choice about continuing or stopping HRT.

- Women who are stopping HRT should be offered the choice of either stopping immediately or gradually reducing their HRT. A gradual reduction may limit recurrent symptoms in the short term.

Vaginal oestrogens

- Women on vaginal oestrogens should stay on treatment for as long as is needed.

- Local oestrogen can be used long term as the 'systemic absorption' of oestrogen from recommended dosages is very small.

- Monitoring of endometrial thickness during treatment is not recommended.

- It is important to report unscheduled vaginal bleeding to the health care professional.

- Women should be advised that symptoms of urogenital atrophy often come back when treatment is stopped.

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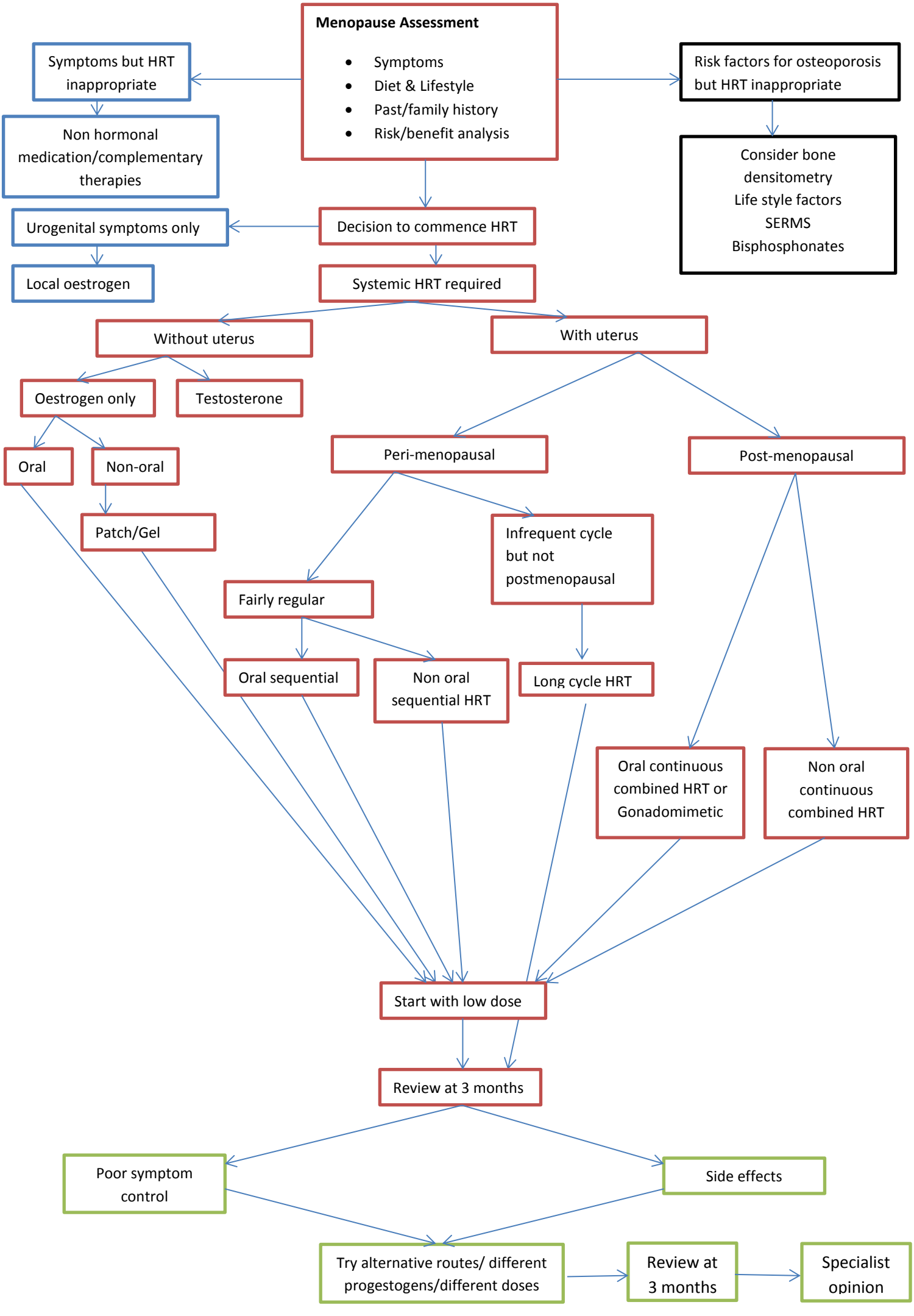
Menopause Assessment
Symptoms
Diet & Lifestyle
Past/family history
Risk/benefit analysis
Symptoms but HRT inappropriate
Non hormonal medication/complementary therapies
Risk factors for osteoporosis but HRT inappropriate
Consider bone densitometry
Life style factors
SERMS
Bisphosphonates
Urogenital symptoms only
Local oestrogen
Decision to commence HRT
Systemic HRT required
Without uterus
With uterus
Oestrogen only
Testosterone
Oral
Non-oral
Patch/Gel
Peri-menopausal
Post-menopausal
Infrequent cycle but not postmenopausal
Fairly regular
Oral sequential
Non oral sequential HRT
Long cycle HRT
Oral continuous combined HRT or Gonadomimetic
Non oral continuous combined HRT
Start with low dose
Review at 3 months
Poor symptom control
Side effects
Try alternative routes/ different progestogens/different doses
Review at 3 months
Specialist opinion