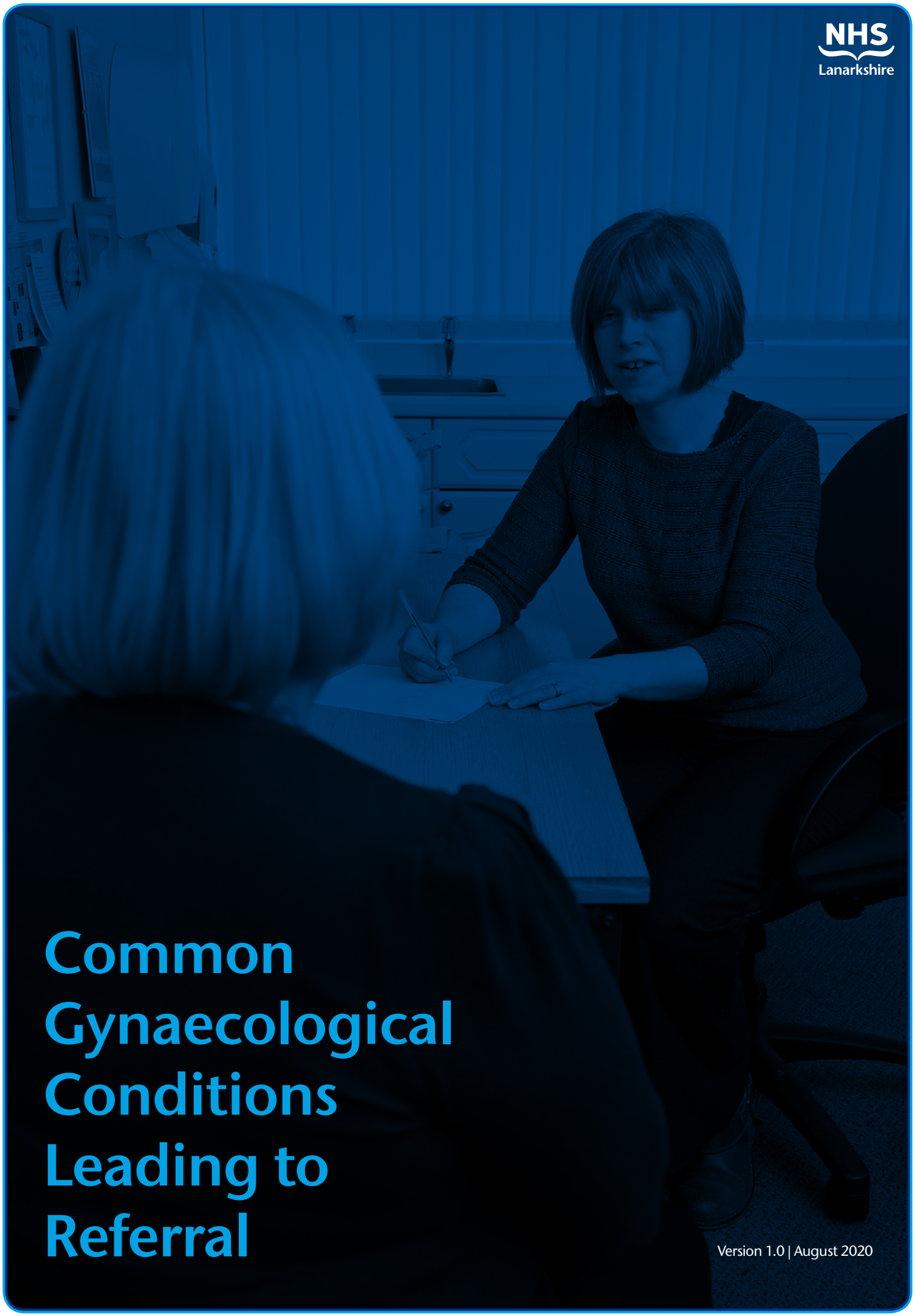
NHS Lanarkshire



Common Gynaecological Conditions Leading to Referral

Version 1.0 | August 2020

Contents

Patients Presenting with Heavy Menstrual Bleeding

HISTORY (Information to aid referral)
See Postcoital/ Intermenstrual bleeding Pathways if primary concern.
Menstrual History; length of cycle, duration of bleeding, heaviness of bleed, IMB, PCB, pelvic pain, pressure symptoms, bowel and urinary symptoms
BMI
Family history of gynaecological, breast or bowel malignancy
INVESTIGATIONS (Include FBC if concerns re anaemia for referral)
FBC
Consider TFT if symptoms present
Consider coagulation profile if family history or persistent HMB since menarche
Arrange USS if no scan in last 12 months
EXAMINATION (Information to aid referral)
Abdominal examination, and consider pelvic examination and smear if due
Consider STI screen if IMB/ PCB or thought to be at risk

Any of the following;
Regular HMB, < 40 years, fibroids <3cm on USS, normal examination

Medical Management in Primary Care
Please consult the BNF prior to prescribing to ensure the choice of medicine is suitable for your patient following discussion of risks vs benefits

Option 1: LNG- IUS for 6 months.

Option 2: Combined oral contraceptive
- a) Rigevidon
- b) Gedarel 30/150
- c) Millinette 30/75

Option 3: Progesterone only pill (off label usage)
- a) Desogestrel
- b) Norgeston
- c) Noriday

Option 4: Progestogen days 5- 26, Norethisterone 5mg tds (beware VTE risk), Medroxyprogesterone 10mg tds (off label usage)

Patients not seeking contraception or wishes non hormonal treatment

Tranexamic acid 1gm tds/qid for 4 days (maximum dose 4g)

Mefenamic acid 500mg tds for 4 days

Review after 3 months for oral therapy
Review after 6 months LNG- IUS

Continue management in primary care

Referral to gynaecology if no improvement in symptoms

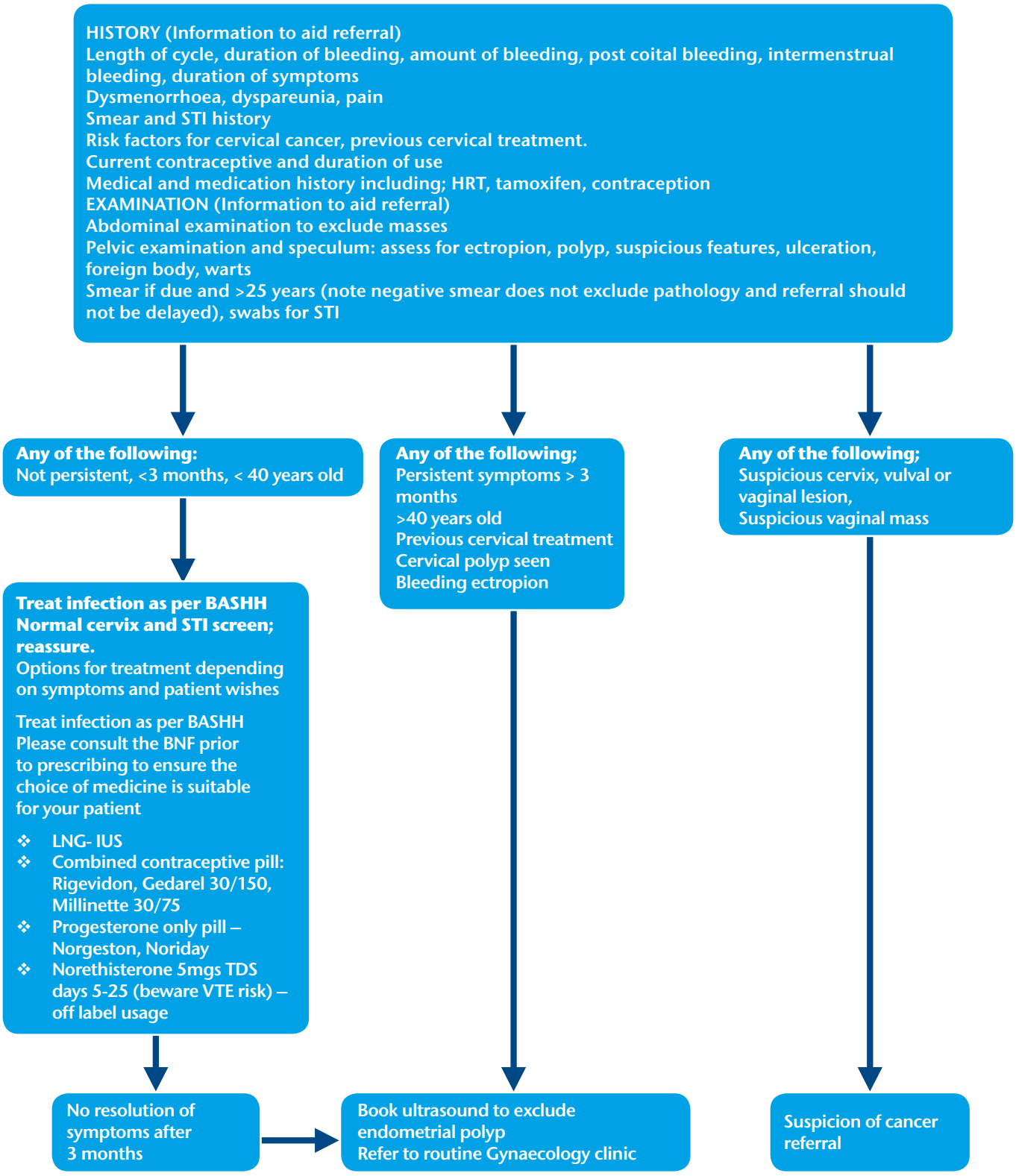
Any of the following;
>40 years with worsening HMB
BMI >30
PCOS
Failed treatment in primary care
Fibroids >3cm on USS

Referral to gynaecology Menstrual Disorders Clinic

Any of the following;
Tamoxifen use
Findings suspicious of cancer
Suspicious, thickened or vascular endometrium on USS

Urgent referral to Gynaecology

Patients presenting with Postcoital and Intermenstrual Bleeding



References

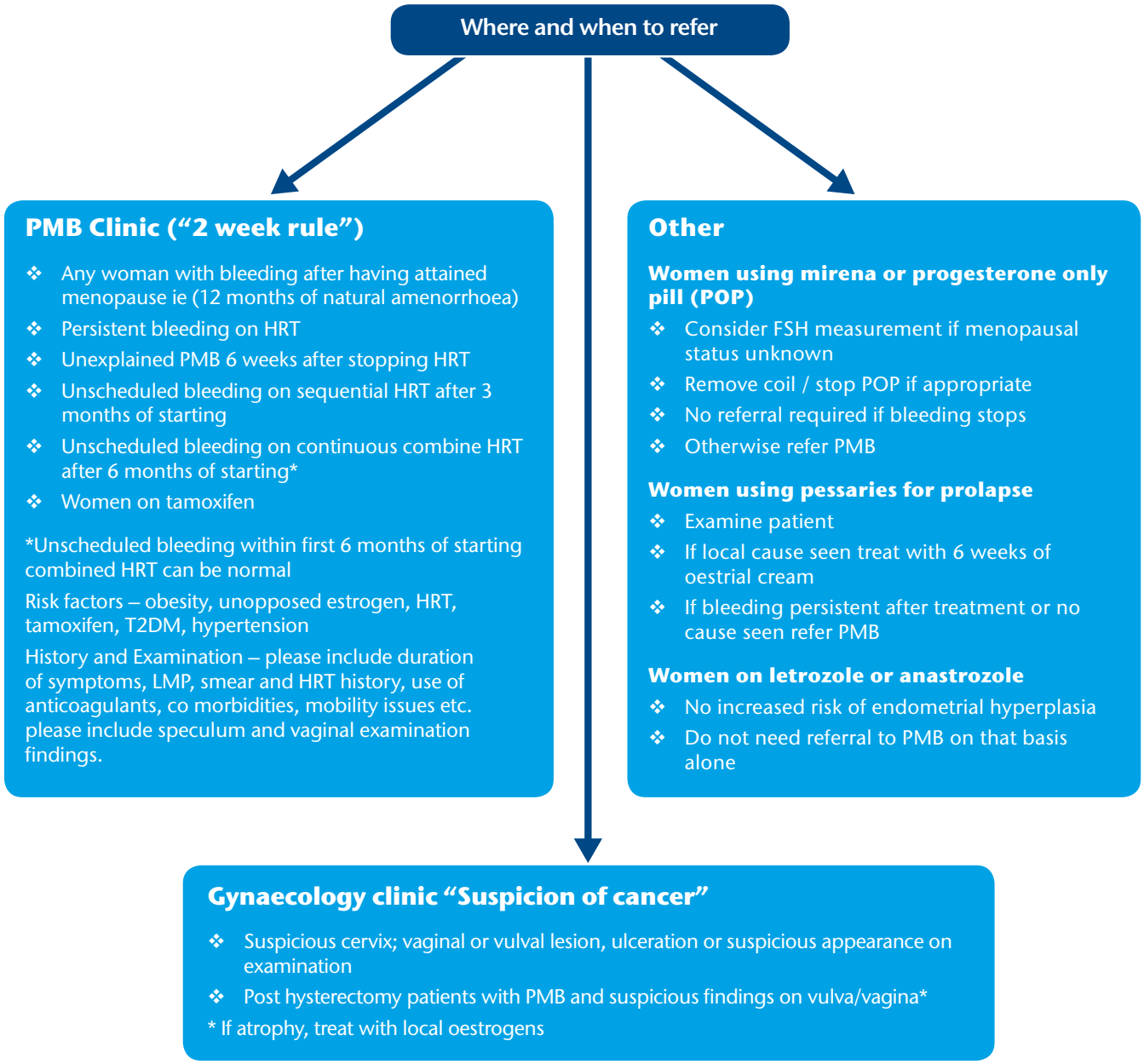
NICE guideline NG88 – Heavy menstrual bleeding - https://www.nice.org.uk/guidance/ng88

https://www.medednhsl.com/meded/nhsl_formulary/index.asp?T=07&S=7.03 – NHS Lanarkshire Formulary

FSRH Clinical Guideline: Problematic Bleeding with Hormonal Contraception (July 2015) – https://www.fsrh.org/standards-and-guidance/documents/ceuguidanceproblematicbleedinghormonalcontraception/

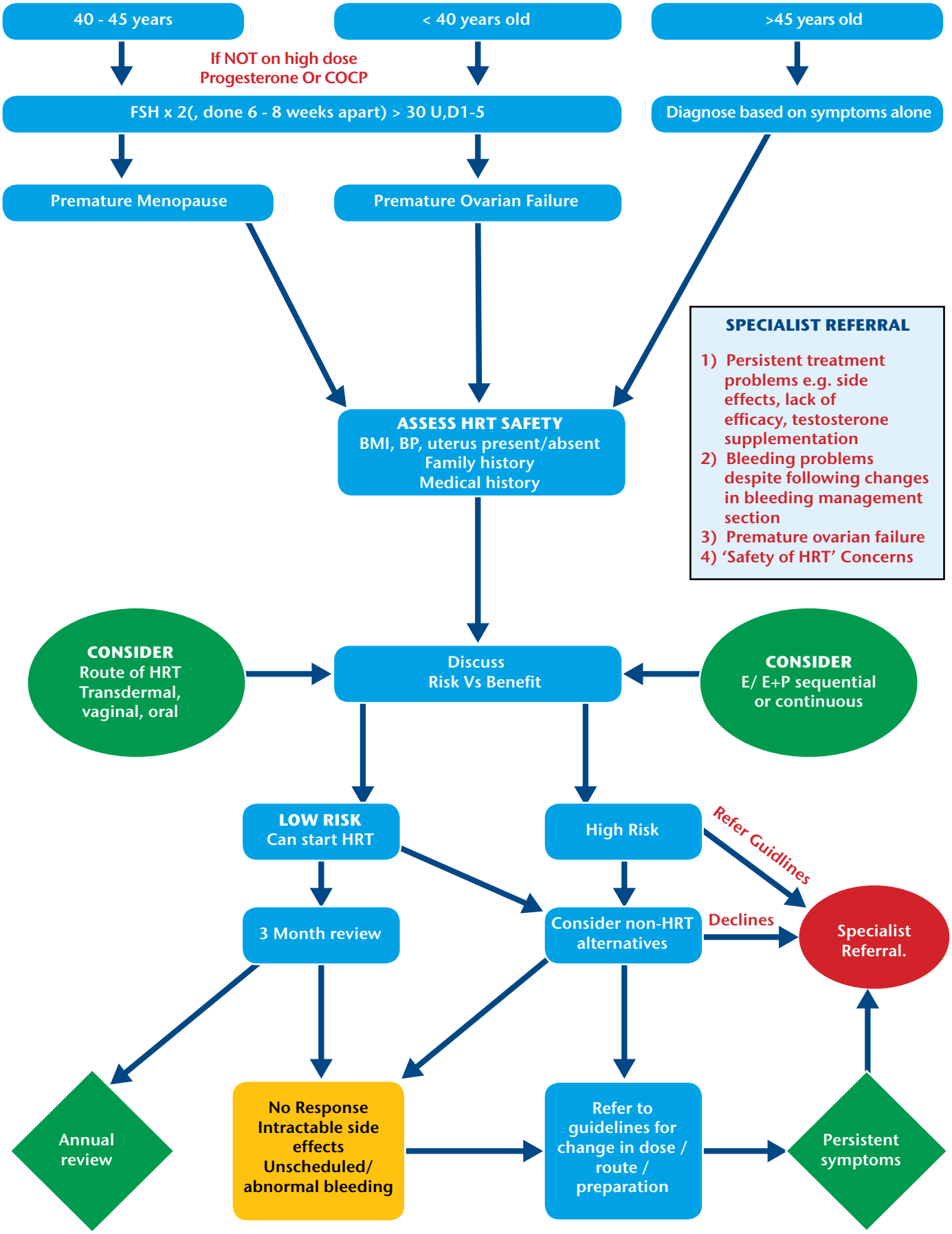
BASHH guidelines – PID https://www.bashhguidelines.org/current-guidelines/systemic-presentation-and-complications/pid-2019/

Patients presenting with Post Menopausal Bleeding



References
Dave, F. G., Adedipe, T., Disu, S., & Laiyemo, R. (2019). Unscheduled bleeding with hormone replacement therapy. The Obstetrician & Gynaecologist, 21(2), 95–101. doi: 10.1111/tog.12553
https://www.nice.org.uk/guidance/ng12/chapter/1-Recommendations-organised by-site-of-cancer#gynaecological-cancers

Patients presenting with Menopausal Symptoms

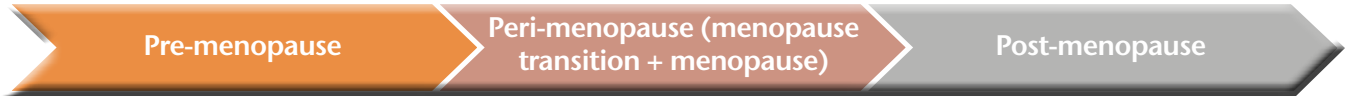


Menopause and HRT

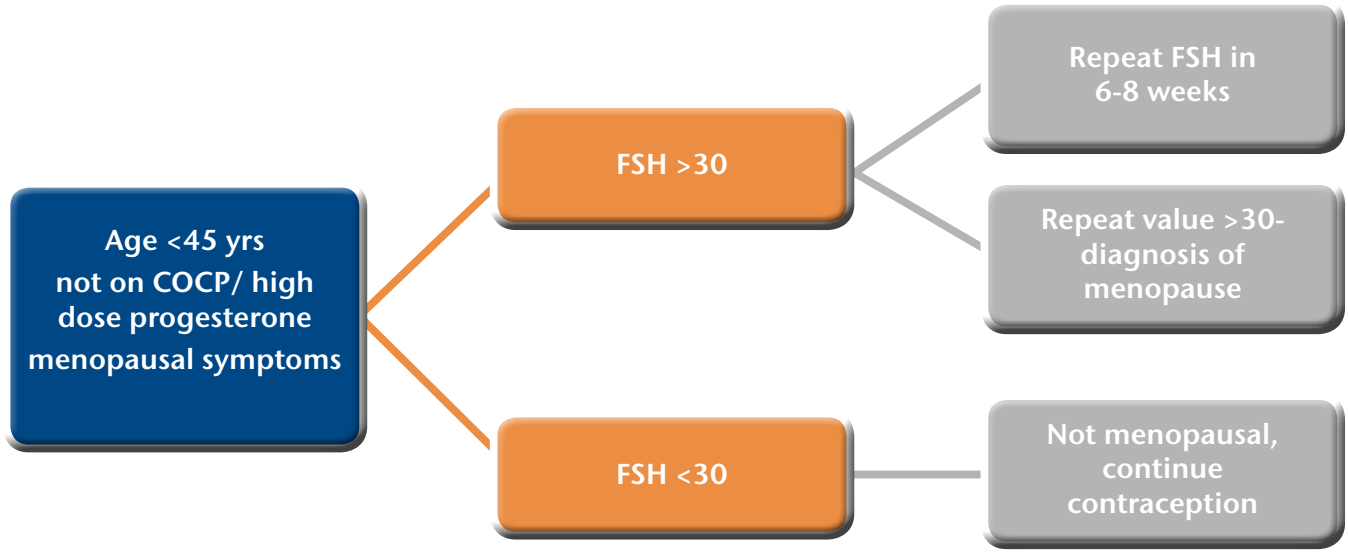
Department of Obstetrics and Gynaecology

University Hospital of Wishaw, Lanarkshire

- Menopause-Permanent cessation of menses. Retrospective diagnosis after 12 consecutive months of amenorrhoea.
- Perimenopause is the stage from the beginning of these menopausal symptoms (irregular menses, vasomotor symptoms) to the menopause (12 months after the last period).
- Early menopause is menopause occurring before age 45 yrs (but after age 40 yrs)
- Premature Menopause or ovarian failure – about 1%-menopause occurring before age 40 yrs (follow POF guidelines)



- Average age of natural menopause in the UK is 51 yrs. It can vary.
- Symptomatic women with cycle irregularity can be clinically diagnosed as entering the menopausal transition. Hypothyroidism or depression may occur in concert during the menopausal transition and should be excluded.
- Testing for a raised serum FSH/LH is not recommended above 45 years of age as the levels are fluctuating and not diagnostic.
- For women <45 yrs, two levels of serum FSH are obtained 6-8 weeks apart. If the woman is still menstruating then the first FSH value should be obtained day 1-5 of the menstrual cycle.
- The diagnosis of menopause can guide the need for contraception. HRT is not contraceptive. Contraception is required for 1 yr after last menstrual period for women >50yrs and 2 yrs for women<50 yrs.

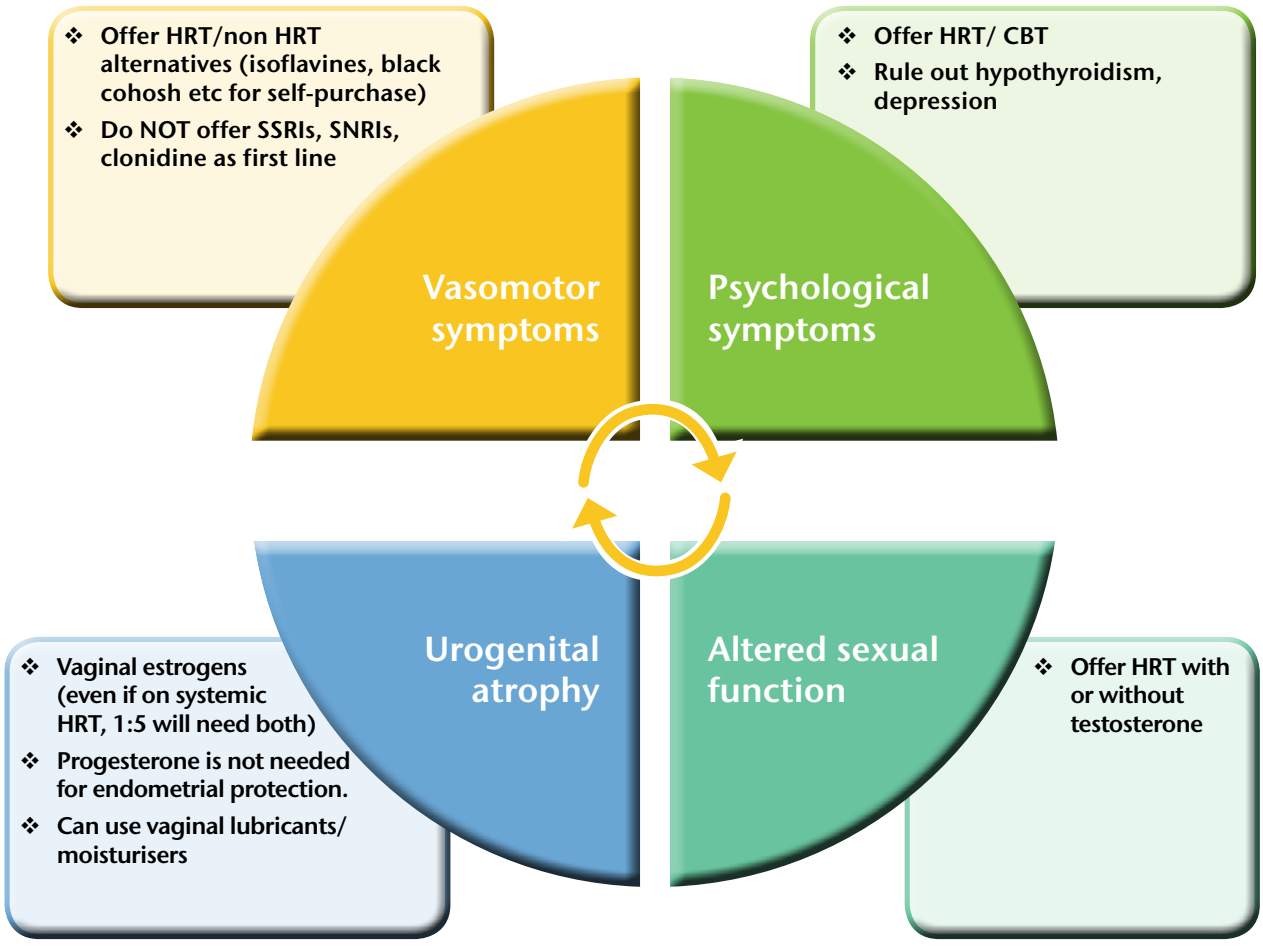


Symptoms of menopause

- About 75-80% of the women will have menopausal symptoms and 25% of these women would find the symptoms severe / affecting quality of life.
- Milder symptoms can respond to lifestyle changes such as weight reduction, exercise, smoking cessation, reducing caffeine and alcohol intake thus not needing medical treatment.
- Severe or persistent symptoms warrant consideration for HRT. Symptoms could be classified as acute, medium and longlasting

acute	medium	longlasting
vasomotor symptoms- hot flushes and night sweats	urogenital atrophy- vaginal dryness, difficulty in intercourse, urinary infections/urgency	Cardiovascular risk
mood swings, irritabilty, emotional lability, insomnia, inability to concentrate	joint pain, headaches, hair loss, brittle nails, dry skin	osteoporosis

There is however evidence to suggest that they may not follow a set time course.



Prescribing HRT

ASSESS
- Gynaecological and smear history
- Family and personal history of malignancy
- Risk of VTE/CVD/ osteoporosis
- Nature and severity of menopausal symptoms
- Need for contraception
- Indications for transdermal HRT as first choice

BMI, BP, migraines, other drugs interaction

ADVISE
- Risks and benefits of HRT
- Lifestyle modifications
- Non-hormonal alternatives (limited data and benefit)
- Routes and types of HRT

ARRANGE
- Serum FSH two values 6-8 weeks apart if < 45 yrs
- Specialist review if concerns about safety of HRT
- Urgent review if suspicion of cancer (abnormal bleeding, new breast lump)
- Follow up in 3 months if started HRT

ASK

Need for specialist advice if:
- Persistent treatment problems e.g. side effects, lack of efficacy, testosterone supplementation
- Bleeding problems despite following changes in bleeding management section (Pg10)
- Premature ovarian failure
- Concerns about safety of HRT

Indications of HRT:
- Intractable menopausal symptoms not responding to lifestyle modification
- Add back therapy with GnRH analogues
- Premature menopause- till natural age of menopause
- Patient choice, QOL

Contraindications of HRT:
- Active breast cancer or endometrial cancer, liver disease
- Myocardial Infarct/ CVD
- Active thromboembolism
- Pregnancy, porphyria

Indications for Transdermal Therapy

- Individual preference
- Poor symptom control with oral
- GI disorder affecting oral absorption
- Previous or family history of VTE
- BMI >30
- Variable blood pressure control
- Migraine
- Current use of hepatic inducing enzymes medication
- Gall bladder disease

General Prescribing Information

- The dose, regimen and duration of HRT need to be individualised (there is no max duration).
- As women get older, generally lower oestrogen doses are sufficient for symptom control. The lowest effective dose should be used.
- Addition of a progestogen is required for protection against endometrial cancer in women with an intact uterus, including those with endometrial ablation.
- It is recommended to start women at the beginning of the menopause on sequential therapy and convert to the continuous method
  - 1 year past the menopause,
  - or when 54 years of age, as almost 80% of women will be postmenopausal at this age
  - or it has been at least two years since their last menstrual period if they had a premature menopause
- Young women often need higher doses of HRT for symptom control (oral oestradiol 3-4mg or transdermal 75-100mcg patches) and to ensure bone and other long term protection.
- HRT should not be used first line in asymptomatic postmenopausal women for primary prevention of osteoporosis or Coronary Heart Disease.

Special Considerations

There are some conditions in which systemic HRT could be only given with caution and after considering getting specialist advice:

- Angina: For women with h/o angina consider non-hormonal therapies initially; Transdermal HRT may be considered after specialist advice; possible increased risk of MI in the 1st year of HRT use; use tools to assess cardiovascular risks
- Diabetes: low dose oestrogen and transdermal preparation preferred
- Thyroid disease: patients on thyroxine should have their TFT rechecked 3 months after starting or stopping HRT to see if dose needs adjusting as HRT affects the thyroid-binding globulin and therefore might decrease free thyroxine; transdermal HRT preferred.
- VTE, thrombophilia or conditions with increased VTE risk (e.g. SLE): consider non-hormonal therapies initially; transdermal HRT may be considered after specialist advice. Family history of VTE: if HRT is used transdermal route is preferred; consider specialist advice (menopause team/haematologist).
- Endometriosis: If HRT started after hysterectomy for endometriosis choice of HRT used should be influenced by extent of endometriosis and continuous combined HRT (at least for the first year postop) might be indicated (discuss with surgeon)
- Sub-total Hysterectomy- Post sub-total hysterectomy– you can give three months of sequential HRT and if no bleeding you can change to oestrogen only HRT (take advice from surgeon) but if any concern about residual endometrium use continuous combined preparation.
- Endometrial ablation- Women who have undergone an endometrial ablation or resection for heavy menstrual bleeding are treated like women with an intact uterus, even if not having any period since the operation (in which case a continuous combined preparation might be tried, irrespective of her menopausal status). A Mirena® IUS is usually contraindicated in these women.
- Fibroids: size of fibroids may rarely increase with estrogen in HRT though not common and it is safe to prescribe. Women who have had uterine artery embolization can safely take HRT.
- Porphyria- HRT and even some of the non- HRT alternatives would be contra-indicated.

Risks counselling for HRT

The risk of HRT is affected by the type, route and duration of use. Continuous progestogens are better for endometrial protection

- **Venous thromboembolism (VTE)**
  - The risk of VTE is increased by oral HRT, particularly in the first year of use.
  - The risk associated with transdermal HRT with standard doses is no greater than baseline population risk.
  - Consider transdermal HRT if woman has VTE risk factors including BMI>30.
  - If high risk of VTE including family history consider referring to specialist service.
- **Cardiovascular disease (CVD) and Stroke**
  - HRT does not increase CVD if started under 60 years or increase risk of dying of CVD.
  - The presence of CVD risk factors is not a contraindication to HRT if they are optimally managed.
  - The risk of coronary heart disease and stroke for women around menopause varies according to her risk factors.
  - Oestrogen-alone HRT does not increase risk of coronary heart disease.
  - HRT with oestrogen and progestogen is associated with little or no increased risk of coronary heart disease.
  - Oral, not transdermal oestrogen is associated with a small increased risk of stroke but in women <60 years the risk is very low. The risk is less likely to be increased if commenced under the age of 60, or within 10 years of the onset of the menopause. Transdermal HRT may be preferable in those with stroke or other CVD risk factors. Micronised progesterone (Utrogestan®-not SMC approved as yet) and dydrogesterone (Femoston® products) may be associated with a lower risk of stroke and CVD.
- **Diabetes**
  - HRT is not associated with an increased risk of developing type 2 diabetes.
  - HRT is not generally associated with adverse effect on blood glucose in women with type 2 diabetes.
  - Consider HRT in women with type 2 diabetes after considering comorbidities and/or seeking specialist advice.
- **Breast cancer**
  - Oestrogen-only HRT is associated with little or no increased risk of breast cancer.
  - Oestrogen and progestogen HRT can be associated with an increased risk of breast cancer, generally the risk is considered low. Micronized progesterone (Utrogestan®) and dydrogesterone may be associated with lower risk of invasive breast cancer.
  - Any increase in risk is related to duration of HRT and reduces after stopping

The risks highlighted below are mainly applicable to women aged over 50 and should not be extrapolated to women with premature ovarian insufficiency (POI) or early menopause in which the benefits of HRT usually outweigh the risks until the age of a natural menopause.

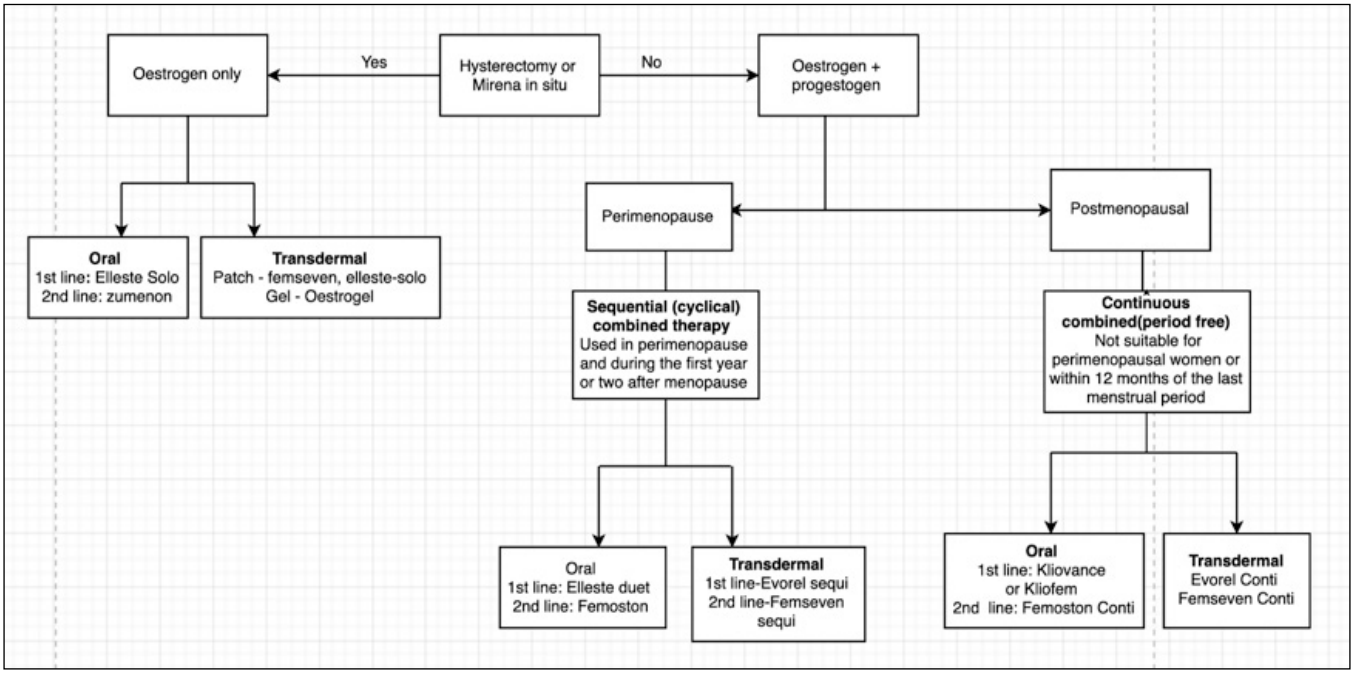
TABLE-Number of cases of disease per 1000 women aged 50-59 over 7.5 years with or without systemic HRT

	No systemic HRT use	Oestrogen-only HRT	Combined HRT
Breast cancer *	22.5	4 fewer	5 more
Cardiovascular disease *	26	6 fewer	5 more
Stroke *	11	no change	6 more
Venous thrombo-embolism **	1.7	4 to 6	4 to 6

* Data summarised from RCTs, NICE Menopause Guideline (NG23)

** https://thebms.org.uk/_wprs/wp-content/uploads/2016/04/HRT-Guide-160516.pdf

Prescribing HRT



The NHSL formulary can be accessed here - https://www.medednhsl.com/meded/NHSL_Formulary/index.asp

Choosing Progesterone in HRT

Class	Examples	Comment
Synthetic- C19 Testosterone analogues	Norethisterone Norgestrel Levonorgestrel	- Good cycle control - Androgenic - Unfavourable effect on lipids - Only available in combined oral or transdermal preparations as HRT - Systemic absorption of levonorgestrel in women using the Mirena® IUS is minimal
Synthetic- C21 Progesterone analogues	Medroxyprogesterone acetate (MPA) (Provera®)	- Androgenic - Unfavourable effect on lipids - Available as combined HRT or as single tablets for endometrial protection of women on transdermal or oral estradiol - Can be used as progestogen – only HRT (unlicensed)
	Dydrogesterone	- Non-androgenic - Possibly associated with less breast ca, VTE and CVD risk - Currently only available in combined oral HRT
"Bioidentical"	Micronised progesterone (Utrogestan®)	- Fewer side effects - Non-androgenic - No effect on lipids - Possibly associated with less breast ca, VTE and CVD risk - Possibly less effective cycle control - Can be used as progestogen – only HRT (unlicensed) - Can be used vaginally at night (un-licensed), especially if there are side effects - Currently not recommended by the SMC

Utrogestan® (micronised progesterone) is a bioidentical oral progestogen which has a reputation of less progestogenic side effects and might have a lower VTE, CVD and breast cancer risk in comparison to Provera® (medroxyprogesterone acetate-MDA) tablets. However, this progestogen is associated with less bleeding control. The recommended dosage is 200 mg orally at night on day 15-26 of a 28-day cycle for sequential HRT or 100 mg orally at night for continuous HRT (unlicensed). Utrogestan® is not recommended by the Scottish Medicines Consortium (SMC).

Duavive® is a new type of HRT which pairs conjugated oestrogen (CE) with a selective oestrogen receptor modulator (SERM) called bazedoxifene acetate. It does not contain a progestogen and is indicated for postmenopausal women with a uterus who are intolerant of progestogens. Duavive® is not recommended by the Scottish Medicines Consortium (SMC), due to non-submission and no longer available. Utrogestan, Cyclogest (200/400mg pessaries) , crinone (8%) gel are other progesterone preparations available in Lanarkshire formulary but are un-licenced for HRT use. Where a primary care prescriber is asked to take on the prescribing, completion of a form C PC maybe requested to complete this.

MIRENA® IUS

- Intra-uterine system (used in combination with oestrogen only HRT). No monthly bleeds.
- Provides contraception. IUS only licensed for 4 years if used as part of HRT (FRSH guidelines -5 years). Jaydess®, Kyleena® are not licensed for endometrial protection.
- Possibly reduced risk of endometrial cancer as with continuous combined HRT (ccHRT)
- Breast cancer risk –insufficient data. Likely to be low.

Testosterone and HRT

At present, there is no licensed product for women (available products are for licenced for men) as testosterone patches and implants have been withdrawn for commercial reasons. NICE recommends testosterone supplementation for menopausal women with low sexual desire when HRT alone is not effective. Patients needing testosterone will need referral to secondary care. Transdermal testosterone in the form of gels can be used in about one tenth of doses licensed for men could be used for women. Tostran® 2% is a gel in a pump dispenser, and one measured pump (which contains 10 milligrams of testosterone) is usually used three times a week. Testogel® is a 5 gm sachet containing 50 mg testosterone gel. A pea- size amount can be rubbed onto lower abdomen and thighs. One sachet should last around 10 days. It can sometimes take a few months for the full effects of testosterone to work; a 3-6 month trial is often recommended.

Gonadomimetics- e.g TIBOLONE/LIVIAL

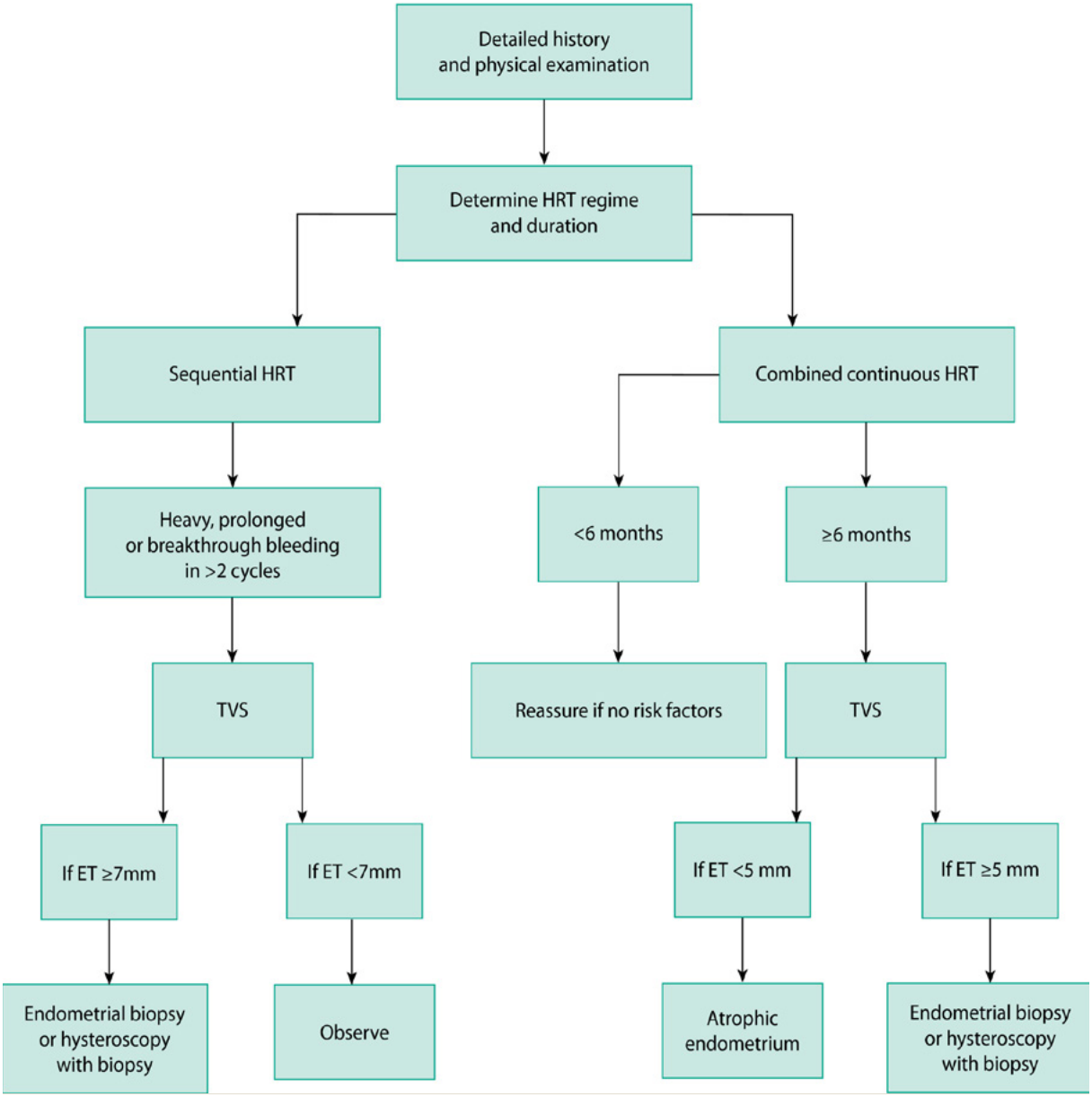
- **Synthetic compound with oestrogenic, progestogenic and androgenic compounds.**
- **No monthly bleeds, does not affect endometrium**
- **Beneficial effect on libido.**
- **Similar indications as continuous combined HRT (ccHRT), including 'add-back HRT' for women on long term GnRH.**
- **Unlike other ccHRT may not reduce the risk of endometrial cancer. Insufficient data.**
- **Breast cancer risk comparable to oestrogen-only HRT and less than ccHRT**
- **Ovarian cancer, venous thrombosis, and coronary heart disease risk –insufficient data.**
- **Stroke: significantly increased risk about 2.2 times from first year of treatment: additional 9 cases per 1,000 age 50-59 years additional 20 cases per 1,000 age 60-69 years**

Managing abnormal bleeding on HRT

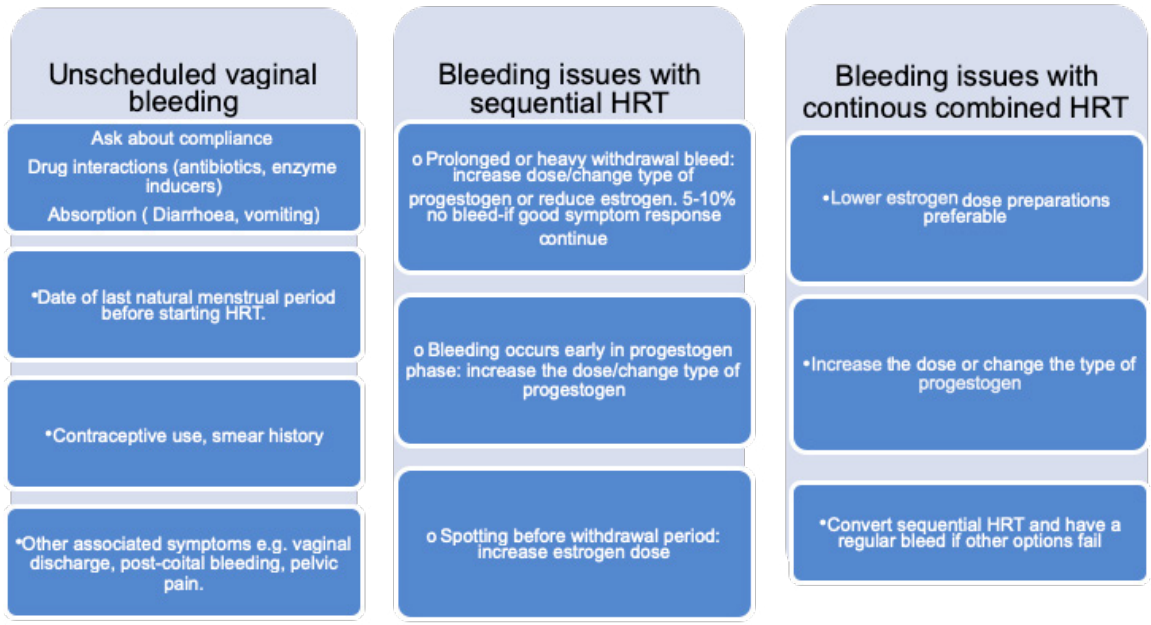
Irregular bleeding during the first six months of HRT use is common and does not usually require referral for investigation at this stage.

Combined continuous HRT use in premenopausal women is not dangerous but may lead to irregular bleeding due to residual endogenous ovarian activity therefore a sequential preparation is more appropriate.

Unscheduled bleeding with hormone replacement therapy



The Obstetrician & Gynaecologist, Volume: 21, Issue: 2, Pages: 95-101, First published: 16 January 2019, DOI: (10.1111/tog.12553)



Referral to PMB clinic

The incidence of endometrial cancer in women with post-menopausal bleeding is approximately 10% up to age 60 years.

The true incidence of endometrial cancer in women with unscheduled bleeding on combined HRT is unknown but a cautious baseline estimate of 1% is assumed.

Indications for referral to specialist clinic to exclude endometrial pathology while on HRT:

- Persistent unscheduled bleeding after the first six months of start or change of HRT
- Any bleeding after amenorrhoea has been established in continuous combined therapy users or persisting 6 weeks after stopping.
- Heavy or prolonged bleeding or bleeding associated with pain in sequential HRT users.

Side effects of HRT and how to manage them

- Up to 35 % of women discontinue HRT due to side effects. It is advised to persist taking it for 3 months as most symptoms would resolve with continued use.
- Medical review is recommended after three months of start or change of HRT followed then by annually for continued assessment of the risks benefits of continuing HR

- Lack of efficacy

Causes
Consider the following causes - Too soon for symptom response - Oestrogen dose not high enough - Patient compliance poor - Limited absorption/metabolism - Woman anxious about taking HRT - Symptoms not menopausal

How long does HRT takes to work?

Vasomotor symptoms—some improvement after one month, maximum by 3 months

Urogenital symptoms— some improvement by 3 months, but may take 6 months

Psychological symptoms—variable response

- Side effects
  - Oestrogen and progestogen can both cause side effects, the cause is more difficult to distinguish in continuous combined preparations.
  - Generally progestogen side effects are more problematic than oestrogen, note the two groups of progestogens (see below) as some women may tolerate one type better than the other.
  - There is no evidence that HRT causes weight gain. However on average women gain 10kg between 40-60 years independently of menopause.

Oestrogen side effects	
Breast tenderness Nipple sensitivity Bloating Leg cramps Nausea/heartburn Headaches	Wait—side effects generally settle <3 months If side effects severe, lower dose Change route i.e. from oral to transdermal
Progestogen side effects	
PMS type symptoms Mood changes Breast tenderness Bloating Headaches Mood changes Acne/greasy skin	Change type of progestogen Change route e.g. oral to transdermal Change regime - consider long cycle HRT or continuous combined HRT , perhaps with IUS to provide progestogen Ask advice from Oxford Menopause Service

Types of progestogens

Progestogens are synthetic forms of progesterone, there are two main groups derived from either

- **testosterone** *(norethisterone, levonorgestrel, norgestrel)*
- **progesterone** *(dydrogesterone, medroxyprogesterone acetate)*
- **other options**
  drospirenone—only available in Angeliq
  micronized progesterone (Utrogestan)

Comparative doses

These are a rough guide as absorption varies

1mg oral oestradiol=25mcg patch=0.5g Sandrena gel

2mg oral oestradiol=50mg patch=1g Sandrena gel

4mg oral oestradiol=100mcg patch=Sandrena licenced to 1.5g

Equivalent doses of conjugated equine oestrogen to oestradiol are not clear

NB The right dose is the lowest to control symptoms/provide bone protection. Younger women tend to need higher doses.

Minimum bone protective doses	
HRT	Dose
Oestradiol oral	1-2mg
Oestradiol patch	25-50mcg
Oestradiol (Sandrena gel)	1g
Conjugated equine oestrogens	0.3-0.625mg

Non-Hormonal Alternatives

Lifestyle modifications like diet optimisation, exercise, reducing caffeine, alcohol helps with menopausal symptoms and general wellbeing:

- Not enough evidence to back efficacy and safety of soy, red clover & black cohosh; more trials are required.
- Some herbal remedies, such as St John's wort, interact with prescription medicines such as anticoagulants, antihypertensives, antidepressants, antiepileptics and contraceptives with potentially serious consequences. Phytoestrogens have shown some benefit but less than traditional HRT.
- Complementary therapies such as Cognitive Behavioural Therapy, acupuncture, acupressure, aromatherapy, Reiki, reflexology may benefit various symptoms associated with the menopause.

Selective serotonin and noradrenaline reuptake inhibitors (unlicensed for HRT use)

- SSRIs (fluoxetine and paroxetine) and SNRIs (venlafaxine) can be effective in reducing hot flushes. Fluoxetine/paroxetine are licensed for menopausal symptoms in women with breast cancer (except those taking tamoxifen). Venlafaxine is not licensed for menopausal symptoms but this use is recognised in various guidelines.
- Venlafaxine is given at a dose of 37.5 mg twice daily. A greater reduction in hot flushes is seen at higher doses but the side effects such as nausea, dizziness, problems with sleeping, agitation and confusion limit dosage.
- SSRIs paroxetine and fluoxetine should not be offered to women with breast cancer who are taking tamoxifen due to interaction.

NICE recommends that they must not be prescribed routinely to alleviate vasomotor symptoms in the absence of a clear diagnosis of depression

- Gabapentin and pregabalin have shown efficacy for hot flush reduction [unlicensed] when compared with placebo but risk of drug dependence. Side effects include drowsiness and fatigue.

Alpha-2 agonists

- Clonidine -although popular to control hot flushes NICE does not recommend it as first line for women presenting primarily with vasomotor symptoms as there is not much evidence to support its use. Its side effects include– dry mouth, dizziness, postural hypotension, sleep disturbances, hallucination, constipation, and sedation.

In a woman with hypertension, clonidine might be considered as initial therapy.

Stopping HRT:

- Gradually reducing HRT may limit recurrence of symptoms in short term but not in the long term.
- Consider reducing the oestrogen dose if changing a woman to a continuous combined HRT from a cyclical, reducing again 1-2 years later.

NHSL Formulary

Extract below from NHSL formulary (August 2020). Up to date formulary information can be accessed at https://www.medednhsl.com/meded/NHSL_Formulary/index.asp [chapter 6.04.01].

Prescribing notes

The MHRA advises that HRT should only be prescribed to relieve post-menopausal symptoms that are adversely affecting quality of life. Treatment should be reviewed regularly to ensure the lowest effective dose is used for the shortest duration. For osteoporosis, consider alternative treatments. HRT does not prevent coronary heart disease or protect against a decline in cognitive function and it should not be prescribed for these purposes. Experience of treating women over 65 years with HRT is limited.

HRT increases the risk of venous thromboembolism, stroke, endometrial cancer (reduced by a progestogen), breast cancer, and ovarian cancer; there is an increased risk of coronary heart disease in women who start combined HRT more than 10 years after menopause.

In August 2019, new data confirmed that the risk of breast cancer is increased during use of all types of HRT, except vaginal estrogens. It was also shown that an excess risk of breast cancer persists for longer after stopping HRT than previously thought (MHRA Drug Safety Update August 2019). Prescribers are advised to discuss the updated total risk with women using HRT.

MHRA Patient Information Sheet - 'Hormone replacement therapy and risk of breast cancer' https://assets.publishing.service.gov.uk/media/5d68d0e340f0b607c6dcb697/HRT-patient-sheet-3008.pd

Please note - due to ongoing HRT shortages this formulary section may be subject to change

Key

P	Preferred list: first-line formulary choices.
T	Total list: alternative choices when preferred list options are not effective / not tolerated.
S1	Specialist initiation, or on the advice of a specialist in gynaecology. Continuation in primary care is acceptable.
S2	Specialist use only. Supply via hospital, not primary care.
*	BNF link

Estradiol only		
P	Evorel• transdermal patch* Strength 25 mcg/24 hours 50 mcg/24 hours 75 mcg/24 hours 100 mcg/24 hours	Twice weekly change
P	Elleste solo• 1mg & 2mg tablets*	*Current supply disruption – possible alternative is Zumenon• 1mg & 2mg tablets*
T	Oestrogel• 0.06% transdermal gel*	Indicated for women without a uterus. In women with an intact uterus it is recommended to add a progestogen (e.g. a progesterone) for at least 12 days of each month, in accordance with the manufacturers' recommendations.
T	FemSeven• transdermal patch* Strength 50 mcg/24 hours 75 mcg/24 hours 100 mcg/24 hours	Once weekly change *Current supply disruption - possible alternative is Elleste Solo MX• transdermal patch (twice weekly change)*

P	Evorel Conti• transdermal patch* **Strength** Estradiol 50 mcg/24 hours and norethisterone 170 mcg/24 hours.	Twice weekly change
P	Kliovance• tablets* **Strength** Estradiol 1 mg and norethisterone 0.5 mg.	One tablet daily without interruption, preferably at the same time every day.
P	Kliofem• tablets* **Strength** Estradiol 2 mg and norethisterone 1 mg.	One tablet daily without interruption, preferably at the same time every day.
T	FemSeven Conti transdermal patches **Strength** Estradiol 50 mcg/24 hours and levonorgestrel 7 mcg/24 hours.	Once weekly change *Current supply disruption*
T	Femoston Conti• tablets* **Strength** **0.5mg/2.5mg** 0.5mg estradiol and 2.5mg dydrogesterone. **1/5mg** 1mg estradiol and 5mg dydrogesterone.	One tablet daily without interruption.

Topical vaginal oestrogen		
P	Estriol 0.1% cream (Ovestin•)*	Excipients: cetostearyl alcohol (including cetyl and stearyl alcohol), polysorbates. One applicator-dose holds 0.5g of cream containing 0.5 mg estriol.
T	Estradiol 10mcg pessary (Vagifem•)*	Available as Vagirux® or Vagifem®. Vagirux® is currently more cost-effective
T	Estradiol 7.5 microgram per 24 hour vaginal delivery system (Estring•)*	Replace after 3 months. Maximum duration of continuous treatment is 2 years.
S[2]	Estriol 0.01% cream	May contain arachis (peanut) oil, cetostearyl alcohol (including cetyl and stearyl alcohol) and polysorbates. One applicator-dose holds 5ml of cream containing 0.5mg estriol.

Progestogen as part of HRT		
P	Levonorgestrel 20 microgram per 24 hour intrauterine device (Mirena•)*	Effective for 4 years.
T	Medroxyprogesterone acetate tablets (Provera•)*	10 mg daily for the last 14 days of each 28-day oestrogen HRT cycle.

P	Evorel Conti® transdermal patch* **Strength** Estradiol 50 mcg/24 hours and norethisterone 170 mcg/24 hours.	Twice weekly change
P	Kliovance® tablets* **Strength** Estradiol 1 mg and norethisterone 0.5 mg.	One tablet daily without interruption, preferably at the same time every day.
P	Kliofem® tablets* **Strength** Estradiol 2 mg and norethisterone 1 mg.	One tablet daily without interruption, preferably at the same time every day.
T	FemSeven Conti transdermal patches **Strength** Estradiol 50 mcg/24 hours and levonorgestrel 7 mcg/24 hours.	Once weekly change *Current supply disruption*
T	Femoston Conti® tablets* **Strength** **0.5mg/2.5mg** 0.5mg estradiol and 2.5mg dydrogesterone. **1/5mg** 1mg estradiol and 5mg dydrogesterone.	One tablet daily without interruption.

Topical vaginal oestrogen		
P	Estriol 0.1% cream (Ovestin®)*	Excipients: cetostearyl alcohol (including cetyl and stearyl alcohol), polysorbates. One applicator-dose holds 0.5g of cream containing 0.5 mg estriol.
T	Estradiol 10mcg pessary (Vagifem®)*	One tablet nightly for 2 weeks then twice weekly maintenance.
T	Estradiol 7.5 microgram per 24 hour vaginal delivery system (Estring®)*	Replace after 3 months. Maximum duration of continuous treatment is 2 years.
S[2]	Estriol 0.01% cream	May contain arachis (peanut) oil, cetostearyl alcohol (including cetyl and stearyl alcohol) and polysorbates. One applicator-dose holds 5ml of cream containing 0.5mg estriol.

Progestogen as part of HRT		
P	Levonorgestrel 20 microgram per 24 hour intrauterine device (Mirena®)*	Effective for 4 years.
T	Medroxyprogesterone acetate tablets (Provera®)*	10 mg daily for the last 14 days of each 28-day oestrogen HRT cycle.

Other		
T	Tibolone 2.5mg tablets*	Short-term treatment of symptoms of oestrogen deficiency (including women being treated with gonadotrophin releasing hormone analogues).

Non-hormonal vaginal moisturiser		
P	Sylk 40g tube	
T	Regelle applicators	Reserved for patients requiring an applicator. Each application lasts for up to 3 days. 6 single use pre-filled applicators = up to 18 days' supply

MHRA Risk Assessment HRT

	Risks over 5 years use (with no use or 5 years current HRT use)		Total risks up to age 69 (after no use or after 5 years HRT use[1])			Risks over 10 years (with no use or 10 years current HRT use)		Total risks up to age 69 (after no use or after 10 years HRT use[1])	
	Cases per 1000 women with no HRT use	**Extra cases per 1000 women using HRT**	Cases per 1000 women with no HRT use	**Extra cases per 1000 women using HRT**		Cases per 1000 women with no HRT use	**Extra cases per 1000 women using HRT**	Cases per 1000 women with no HRT use	**Extra cases per 1000 women using HRT**
Risks associated with **combined estrogen-progestogen HRT**									
Breast cancer	13	**+8**	63	**+17**		27	**+20**	63	**+34**
Sequential HRT	13	**+7**	63	**+14**		27	**+17**	63	**+29**
Continuous combined HRT	13	**+10**	63	**+20**		27	**+25**	63	**+40**
Endometrial cancer	2	-	10	-		4	-	10	-
Ovarian cancer	2	**+ <1**	10	**+ <1**		4	**+1**	10	**+1**
Venous thromboembolism (VTE)[5]	5	**+7**	26	**+7**		8	**+13**	26	**+13**
Stroke	4	**+1**	26	**+1**		8	**+2**	26	**+2**
Coronary heart disease (CHD)	14	-	88	-		28	-	88	-
Fracture of femur	1.5	-	12	-		1	-	12	-
Risks associated with **estrogen-only HRT**									
Breast cancer	13	**+3**	63	**+5**		27	**+7**	63	**+11**
Endometrial cancer	2	**+4**	10	**+4**		4	**+32**	10	**+32**
Ovarian cancer	2	**+ <1**	10	**+ <1**		4	**+1**	10	**+1**
Venous thromboembolism (VTE)[5]	5	**+2**	26	**+2**		10	**+3**	26	**+3**
Stroke	4	**+1**	26	**+1**		8	**+2**	26	**+2**
Coronary heart disease (CHD)	14	-	88	-		28	-	88	-
Fracture of femur	0.5	-	12	-		1	-	12	-

References

1. British Menopause Society: www.thebms.org.uk
2. Menopause Matters: www.menopausematters.co.uk
3. Patient information: www. patient.info/womens-health/menopause
4. NICE overview Menopause: diagnosis and management (https://www.nice.ork.uk/guidance/ng23)
5. www.sexualhealthtayside.org/wp-content/uploads/2018/10/NHS-Tayside-Menopause-Guideline-2018
6. Unscheduled bleeding with hormone replacement therapy.F.G.Dave, T.Adedipe S. Disu, Raphael Laiyemoa. The Obstetrician & Gynaecologist Volume 21, Issue 12, Jan 2019
7. HRT formulary and treatment guidance - Berkshire West CCG,NHS Tayside

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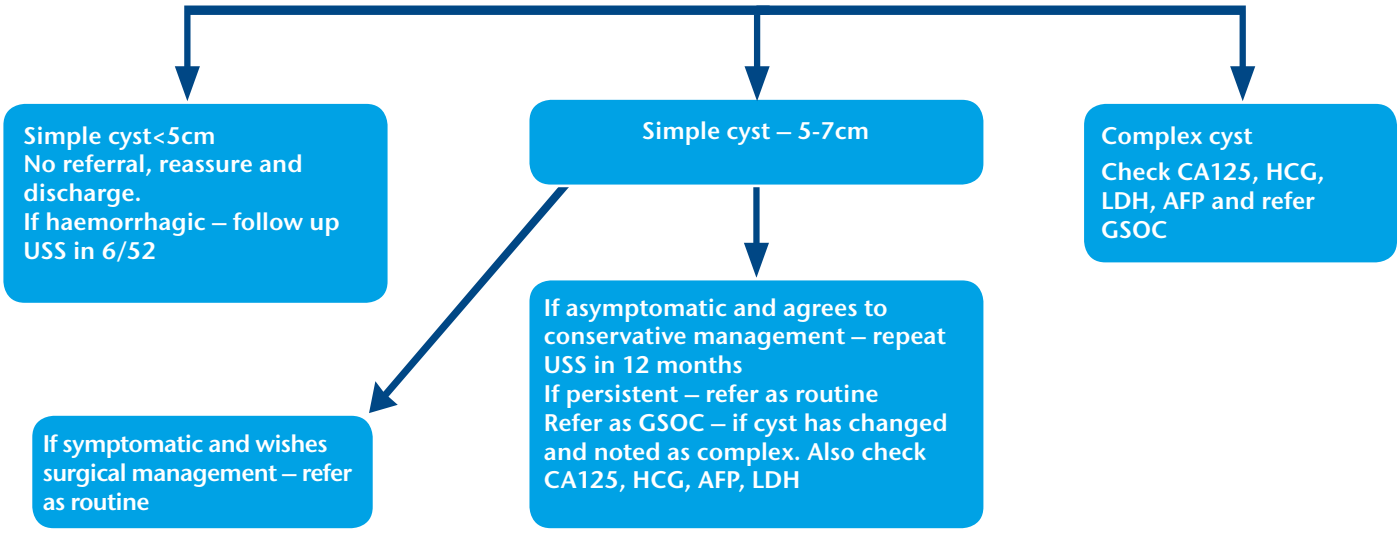
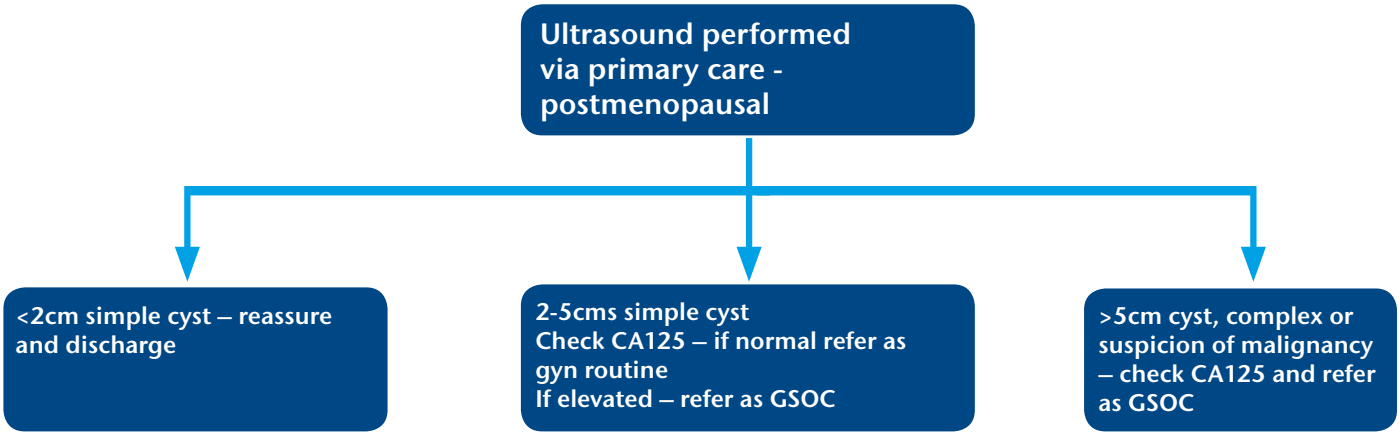
Premenopausal patients presenting with Ovarian Cysts



Postmenopausal patient presenting with Ovarian Cysts



Patients presenting with Pelvic Pain

HISTORY (Information to aid referral)
Pelvic pain, dyspareunia, painful periods
Nature, duration, pattern of pain
Menstrual, bowel and urinary history
Obstetric, Sexual and contraceptive history
EXAMINATION (Information to aide referral)
BMI
Abdominal examination and consider pelvic examination and smear if due
INVESTIGATIONS
Urinalysis
STI screen
Consider pelvic ultrasound

URGENT REFERRAL
Abnormal cervix on examination
Pelvic or abdominal mass
Ca125
USS

SUSPECTED PID
Recent partner change, Recent procedure including coil change, miscarriage, termination or childbirth.
History of PID, ectopic pregnancy

TREATMENT
Positive STI screen
Treat as per BASHH;
Oral doxycycline 100mg BD 14 days + oral metronidazole 400mg BD 14 days + IM ceftriaxone 1000mg single dose
OR
Oral ofloxacin 400mg BD 14 days + oral metronidazole 400mg BD 14 days
https://www.bashhguidelins.org/current -guidelines/systemic presentation-and-complications/pid-2019/
Treat sexual partner

Refer to sexual health

SUSPECTED ENDOMETRIOSIS
Painful periods +/-
Heavy menstrual bleeding
Dyspareunia,
Consider cyclical bladder pain, dyschezia
Partial or complete response to hormonal treatment

TREATMENT 3-6 MONTHS
Review after 3 months, consider trial of second method.
LIFESTYLE ADVICE; stop smoking, optimise BMI, alcohol reduction
NON HORMONAL OPTIONS
Paracetamol ,NSAIDS, Mefanamic acid 500mg tds
MENSTRUAL SUPPRESSION FOR 3 MONTHS
Combined oral contraceptive; Rigevidon, Gedarel 30/150, Millinette 30/ 75
Progesterone only pill; Norgeston, Noriday
LNG- IUS
Depoprovera
Many women will require a combination of hormonal and non hormonal methods

Partial or no response

Refer routine gynaecology

SUSPECTED NON GYNAECOLOGICAL
IBS
Pain related to food, relieved by defecation, bloating, change in bowel habit
BLADDER
Frequency, urgency, incontinence, dysuria
MUSCULOSKELETAL
Worse with movement, improved with rest
Associated abdominal and back pain
NEUROPATHIC
Non cyclical, constant, not limited not limited to pelvis.
Pain not improved with hormonal or surgical method.

TREATMENT
IBS
Dietary and lifestyle measures
Antispasmodics +/- bulking agents
http://www.nice.org.uk/CG61
BLADDER
Consider physiotherapy +/- urological referral
MUSCULOSKELETAL
Physiotherapy referral
Analgesia; paracetamol, NSAIDS
NEUROPATHIC
Offer choice of amitriptyline, duloxetine, gabapentin or pregabalin
http://www.nice.org.uk/CG173

Polycystic Ovary Syndrome

Estimated prevalence of 2-26% in reproductive aged women PCOS is a diagnosis of exclusion and other conditions can cause menstrual irregularities and androgen excess should be ruled out

History suggestive of PCOS

- Infertility
- Obesity
- Oligomenorrhoea (<9 periods a year)/ Amenorrhoea
- Hirsutism
- Acne
- Alopecia
- Family history

Request bloods to include

- Testosterone & SHBG (FAI will be calculated)
- FSH
- LH
- Estradiol
- Prolactin
- HbA1c or random glucose if BMI >30 or FH
- TFTs – if current thyroid status unknown

Unless the patient is amenorrhoeic take sample on day 1-5 of menstrual cycle and include LMP on form

Request pelvic USS only if other indications e.g. pelvic pain or diagnostic uncertainty e.g high clinical suspicion and normal blood

- 33% of women of reproductive age will have polycystic ovaries on USS

Diagnosis of PCOS if 2/3 of the Rotterdam criteria
1. Oligo or amenorrhoea 2. Clinical or biochemical hyperandrogenism 3. Polycystic ovaries on USS

Testosterone: Normal to slightly↑

- If total testosterone >5 nmol/L (or twice upper limit of normal range) exclude androgen secreting tumours and CAH. Refer endocrine.

SHBG: Normal to↓
FAI: Normal to↑
LH:FSH: Not part of clinical criteria but help to exclude other diagnoses

- >2 with normal FSH ?PCOS
- Both increased ?premature ovarian failure
- Both reduced ?hypogonadotrophic hypogonadism

Prolactin: If significantly raised (>750mIU/l) repeat to confirm then investigate causes of hyperprolactinaemia. If >1000 mIU/l discuss with endocrine.

USS: 12 or more follicles in one or both ovaries of 2-9mm diameter +/or increased ovarian volume (>10ml3)
* The syndrome can exist in the absence of polycystic ovaries

PCOS confirmed

- Weight loss for all overweight women – Dietician, Weigh-to-go (Lanarkshire Leisure and Culture) ,metformin not licenced, ltd benefit
- Symptom treatment
- Oligomenorrhoea/amenorrhoea: Cyclical progesterone to induce withdrawl bleed every 3-4 months /COCP
  - Subfertility : refer to infertility services
  - Hirsutism: Cosmetic / Laser (may be considered for NHS funding) / Consider co-cyprindiol
  - Acne: COCP / Consider co-cyprindiol / ref dermatology
- Discuss association with increased risk of T2DM and CVD – weight loss benefits both
- If no improvement of symptoms with above refer gynaecology / endocrinology / dermatology as appropriate

Polycystic Ovary Syndrome

Most women are successfully managed symptomatically in primary care

1. Diagnosis and explanation to patient including written information eg RCOG patient information leaflet Polycystic Ovary Syndrome (PCOS)
2. First line treatment – supportive and lifestyle including diet/exercise etc and management of obesity
3. Management of symptoms

OLIGO/AMENORRHOEA:

- Aim for menses at least every three months FOR endometrial protection
- If contraception not required - periodic progestogen therapy eg medroxyprogesterone acetate 10mg BD for one week or 10mg OD for 10-14 days.
- If contraception required, COCP
- If COCP contraindicated, POP or subdermal implant or Mirena IUS

ACNE

Refer to dermatology guidance for standard management

HIRSUTISM

- First line is cyproterone acetate (CPA) formulated as per COCP (co-cyprindiol 2000/35) unless contraindicated. However other COCPS have similar efficacy.
- Eflornithine cream(Vaniqa) may also be useful. It can irritate the skin but may work faster than CPA.

PSYCHOLOGICAL and PSYCHOSEXUAL ISSUES

Women with PCOS often suffer from low self esteem, thus psychological support can be required.

4. Management of metabolic risks. Women with PCOS are at increased risk for impaired glucose tolerance and T2DM. Weight loss and lifestyle modification is important.

SCREEN FOR T2DM

- BMI ≥ 30
- OR risk factors eg >40 years old, family history, history of gestational diabetes

CONSIDER SLEEP APNOEA

5. When to consider onward referral

To gynaecology ✓

- Diagnostic uncertainty
- More specialist management required e.g. when first line therapy ineffective or contraindicated; bleeding issues despite being on treatment

To other specialty ✓

- Local infertility pathway - when infertility is the primary issue
- Endocrinology - when a repeat testosterone is >5 nmol/l or twice upper limit or normal

Patients presenting with Subfertility

Information for GPs:

- Ideally couples who are having difficulty in conceiving should be seen together prior to referral. (this may not be possible if registered at different practices)
- Full history and examination of both partners should be undertaken if appropriate
- Initial non-invasive investigations are likely to provide useful information prior to referral. (see below for recommended investigations)

Unless an early referral is indicated (as per NICE guidance*), couples should not be referred to fertility services until they have been trying to conceive for at least a year.

Patients unsuitable for referral to Infertility clinic:

Age >42 yrs, BMI>35 (see below for further advice)

Information to provide to patients:

- Cumulative probability of pregnancy in general population is >80% in first year and >90% by end of second year in women under the age of 40 if they are having regular intercourse
- Fertility naturally declines with a woman's age
- Advise sexual intercourse every 2–3 days rather than timing based on menstrual cycle
- Limit alcohol intake to ≤ 1–2 units alcohol/week for women; ≤ 3–4 units/week for men
- Smoking is likely to affect a woman's fertility and may affect a man's sperm quality- encourage smoking cessation. Men should be advised against wearing tight-fitting underwear or testicular hyperthermia
- Aim for Body Mass Index of >18.5 and <30 due to reduced fertility out with this range for both partners
- Women with BMI >30 should be referred to community dietician and referred to Subfertility clinic when BMI < 35
- Recreational drugs should not be taken by either partner
- Psychological stress can contribute to difficulty in conceiving – consider referral to counselling services / psychosexual counselling

Recommend the following pre-conception measures

- Folic acid (400mcg daily) should be taken by women trying to conceive (in some cases a 5mg daily dose is indicated- maternal diabetes, BMI>30, those taking anti-epilepsy medication, previous pregnancy affected by a neural tube defect)
- Rubella immunity is confirmed (If sero-negative offer vaccination and advise not to try for a month)
- Cervical screening is up to date
- Ensure appropriate preconception counselling for women with underlying medical conditions.

Female Investigations:

- Screening for STI by self-taken vulvovaginal swab
- Mid-luteal progesterone (day 21 of 28 day cycle, timing may vary depending on cycle length e.g should be performed at day 28 of a 35 day cycle)

If absent menstruation (anytime) or cycle length >42 days(d1-d4):

- Serum FSH/LH/Estradiol before thyroid function tests
- Thyroid function tests
- Prolactin
- Androgen screen

Male Investigations:

- Semen analysis
- Urine for STI screening

If abnormal then consider referral , if very low- repeat in a month, if border-line repeat in 3 months

Seminal analysis is performed in the Andrology Lab in University Hospital Monklands (phone number 01236 712282) - please provide patient with referral form which contains contact details for department and ask patient to phone to organise appointment.

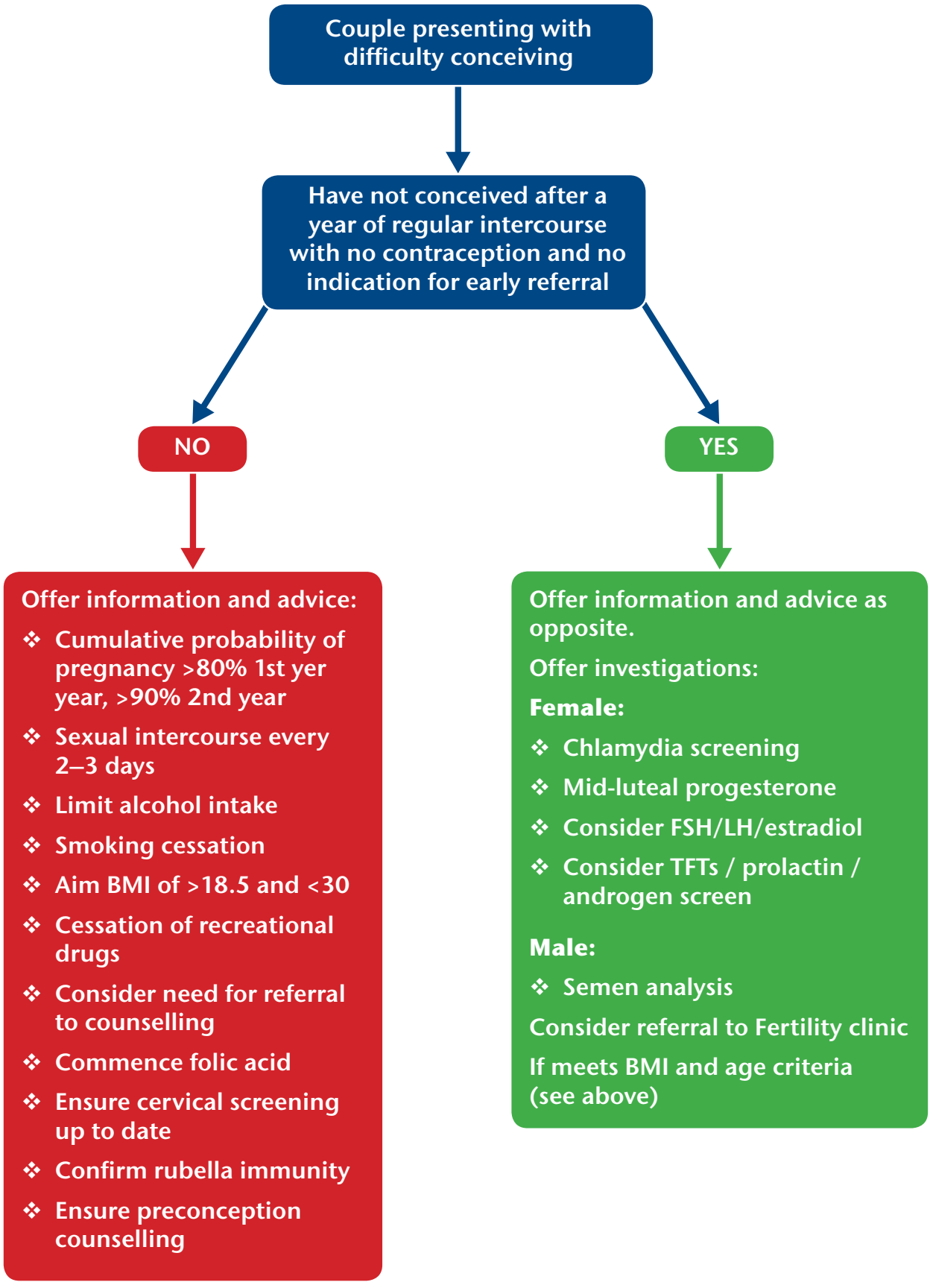
*Indications for early referral to Subfertility clinic:

- Woman age is 35 or over
- There is a known clinical cause of infertility or a history of predisposing factors for infertility such as:
- Amenorrhoea/oligomenorrhoea
- Previous pelvic surgery, h/o undescended testes, testicular surgery/torsion
- Previous PID
- Abnormal investigation results, or for men abnormal semen analysis or other investigations
- Any other significant history, examination or investigation e.g. previous or planned cancer treatment, chronic viral infection
- Same sex couples if cohabiting for 2 years and meeting access criteria can be seen to be referred to tertiary centre for IUI/IVF

Access criteria for assisted conception such as IVF, ICSI, Donor treatments:

- Female partner <39 years at time of referral (possibly 3 cycles of IVF)
- Female partner 39-41 years may be eligible for 1 cycle of IVF
- Either partner previously sterilised ineligible
- BMI for female partner > 18.5 and < 30
- Both partners non smokers
- Both partners abstain from recreational drugs and methadone for one year
- Co-habiting for at least two years in a stable relationship
- Couples where at least one partner has no living biological child
- No welfare of child issues

The criteria for IUI in University Hospital Monklands is similar to above except only offered to women under 39yrs and also offered to couples with secondary infertility.



References
NICE guideline Clinical Guideline (CG156)

Patients presenting with Pelvic Organ Prolapse

Offer Reassurance, lifestyle advice (as below) and suggest referral for PFMT if:

Asymptomatic Mild/ Moderate Prolapse

Symptomatic/ Asymptomatic
History,
Abdominal + Pelvic examination,
urinanalysis +- MSSU

Urgent Referral
(to appropriate service)
Pelvic Mass
Urinary retention
Bleeding
(genital, rectal, urinary)

Routine Referral
Complex multiple symptoms
Severe prolapse at or beyond the introitus

- Lifestyle advice (weight reduction, avoid heavy lifting, manage constipation and chronic cough)
- Consider topical oestrogen if atrophy present
- Supervised pelvic floor muscle training (PFMT) is recommended first line for mild/moderate prolapse
- Consider vaginal pessary in community if available

Routine referal if the above methods are declined, not available, unsuccessful in community

Recommended patient information leaflet link: https://www.rcog.org.uk/globalassets/documents/patients/patient-information-leaflets/gynaecology/pi-pelvic-organ-prolapse.pdf

Female Lower Urinary Tract Symptoms
(Incontinence/Overactive Bladder symptoms)

- Femail Patient with Lower Urinary Tract Symptoms (Incontinence/Overactive Bladder symptoms...)
- History, Examinations, Urinalysis/MSSU
- Exclude/Treat any urinary tract infection

↓

- Refer to Urology if frank/persistent microscopic haematuria or recurrent/persistent urinary tract infection and no history of vaginal mesh insertion

↓

- Refer to Urogynaecology if:

1. History of persisting bladder or urethral pain, vaginal mesh insertion, continence surgery, pelvic surgery or radiation
2. Coexisting (symptomatic prolapse below the vaginal introitus, colorectal symptoms or neurological condition)
3. Findings suggest (pelvic masses, genital fistulae or voiding difficulty/retention)

↓

- Lifestyle modifications (weight reduction if high BMI, ensure good glycaemic control if diabetic and normal fluid intake 1.5-2 L)

↓

- Symptoms dominated by stress incontinence: Refer to Gynaecology and pelvic physiotherapy for supervised pelvic floor muscle training (PFMT)

- Symptoms dominated by urgency, urge UI: Refer to Continence Advisory Service for bladder training & further fluid management advice AND consider trial of Anticholinergic/ Mirabegron (2 at least for 6 weeks each)

↓

- Refer to Urogynaecology if the above measures are unsuccessful/declined

Reference:
Urinary incontinence and pelvic organ prolapse in women: management. NICE guideline [NG132]. Published April 2019. Available at: https://www.nice.org.uk/guidance/ng123

Patients presenting with Vulval Itch/Pain

HISTORY

Duration of itch
Spread; confined to specific area or generalised
Other symptoms; bleeding, discharge, urinary symptom, ulceration or lesion
Effects on sexual function
Medical history; systemic illness, skin disorders, medication
Alteration in cleansing regime pads/ washing powder, etc

EXAMINATION

(to aide referral)
Skin colour changes
New focal lesions
Loss of architecture, skin creases, folds or fusion
Bleeding
Broken skin
Progression of change in vulva

Red flags present?

Yes

Indications for 2WW referral and possible vulval biopsy:

1. Areas of vulval melanosis or new pigmented lesions
2. Persistently eroded areas
3. Indurated and suspicious ulcerated areas
4. Poor response to previous treatments
5. Known previous VAIN/ VIN Rapidly
6. Rapidly progressing lesion

No

Consider trial of empirical treatment and agree follow-up consultation

Follow-up and ongoing care: Women should be encouraged to self-examine regularly and to attend for examination once year https://www.rcog.org.uk/en/patients/patient-leaflets/skinconditions-of-the-vulva/

Suspected Lichen Sclerosus or Planus

Trial of reducing course of dermovate (clobetasol proprionate 0.05%) - nightly for 1 month, alternate nights for 1 month, 2x/ week for 1 month

Suspected atrophy

Sylk or similar lubricant

Topical Oestrogen pessaries or cream-Ovestin, Vagirux every night for 2 weeks then x2/ week 3-6 months

Suspected Vulval Psoriasis or vulval eczema

Trial of Clobetasone butyrate 0.05% BD for 2/52 then taper

Consider association with other autoimmune conditions

Offer FBC, ferritin(20% of dermatitis will improve with correction of ferritin) TFT and DM when available

General advice for all women: Cotton underwear, consider continence issues, advise water only on vulval area or simple emollient/ dermol for cleansing. Note candidiasis can complicate other conditions such as Lichen Sclerosus

If no improvement or worsening symptoms - refer to Gynaecology as routine. If symptoms have improved or resolved with treatment then continue reducing course.

Author List

1. Pelvic Pain: Dr L Kellison
2. Vulval Pain: Dr F Watson, Dr R Kumar, Dr L Kellison
3. Heavy Menstrual Bleeding: Dr E O'Conner, Dr L Kellison, Dr A McLellan, Mr M Smith (Pharmacist)
4. Post coital bleeding: Dr L Kellison, Dr E O'Conner, Ms A Aslam (Pharmacist)
5. Post Menopausal Bleeding: Dr C Kerr- Wilson, Dr A Pandravada, Dr L Kellison
6. Ovarian Cysts: Dr A Pandravada, Dr E O'Conner
7. Polycystic ovarian syndrome- Dr C Kerr- Wilson, Dr S Jain, Dr R Kumar
8. Subfertility: Dr H Narang, Dr S Jain, Dr R Kumar
9. Menopause: both documents: Dr H Narang, Dr S Jain, Ms K Maroni (Advanced Pharmacist), Pamela Miller (Pharmacist), Rebecca Ritchie (Pharmacist)
10. Prolapse: Dr A Hassan, Dr K Rana, Dr A Duncan, Dr R Kumar
11. Urinary Incontinence: Dr A Hassan, Dr K Rana

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