PRIMARY CARE

MED437

WOMEN'S HEALTH

Objectives:

- Describe gender variations in the risks of common medical conditions and clinical presentations eg CVD, Psychiatric conditions.. etc
- List different contraceptive options and describe a comprehensive approach to assessing the suitability of each method's use, expected side effects and contraindications.
- Identify and discuss the changes pregnancy, postpartum and breastfeeding have on a woman and the role Family doctors play.
- Demonstrate an approach to counseling women on Osteoporosis: prevention, screening, diagnosing and therapeutic strategies.
- Understand the menopause transition and determine the related symptoms , health problems and therapeutic strategies
- Describe a comprehensive approach to gender specific screening. (The details of condition specific screening strategies including chronic disease and cancer will be covered in separate lectures)

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References

- Doctor's slides and notes

Important *Notes* *Extra* *Golden*

Editing file link

1-Contraception

Terminology:

- **Monophasic OCs**: contain a fixed amount of estrogen and progestin throughout the entire cycle.
- **Biphasic**: contain a fixed amount of estrogen while the progestin content increases in the second half of the cycle.
- **Triphasic**: may have a fixed or variable amount of estrogen along with a dosage of progestin that varies in 3 phases.

Overview:

- Ethinyl estradiol (EE) and mestranol are the two types of estrogen used in OCs.
- OCs contain 1 of 7 different progestins.
- The pill is said to be 99.9% effective although the typical user failure rate is about 3%
- Efficacy is compromised by missed or delayed doses, drug interactions, illness affecting GI absorption (vomiting, diarrhea, IBD), other patient variables (eg. smoking).

Choosing an OC

- For most young healthy women without comorbid disease, contraindications, or major risk factors, an OC with the lowest effective hormone dose should be prescribed initially for a trial of 3 months
- Although the monophasics are thought to have better cycle control with less breakthrough bleeding (BTB) than the triphasics, by the 4th cycle all products are basically equivalent regardless of phasic formulation or progestin content.
- Smoking and delayed or missed doses probably have a more significant impact on BTB than product formulation.

What is important in contraception consultation?

Risk factors
Patient's preference
Life circumstances

Starting Hormonal Contraceptives

1. Starting Combined OCs:

- **most effective if started Day 1 of menstrual period**
- can be started any day up to Day 6
- to avoid wknd periods, start on first Sunday after period begins
- **If started after Day 5 use backup method for first 7 -10 days** as ovulation may not be suppressed

2. Starting Progestin-only Pill (POP):

- start on Day 1 of menstrual period and daily thereafter
- use backup method for first month

3. Starting Depo-Provera:

- should be injected during the first 5 days of menstrual cycle to rule out pregnancy
- repeat injection q3 months (12 weeks)
- effective for up to 14 wks

4. Starting Norplant:

- insert within the first 7 days of menstrual cycle to rule out pregnancy
- must be removed and replaced after 5 yrs

EXTRA :

How to take the pill

You may begin taking your birth control pills in 1 of 3 ways:

- **Sunday Start cycle**: Start your first pack of birth control pills on the Sunday during or immediately following your menstrual period. Thus, if your period starts on a Sunday, you start the birth control pill that day ***OR***
- **Day 1 Start cycle**: Start your first pack of pills the same day your period starts. Thus if your period starts on a Tuesday, you start the birth control pills that day.
- **Day 5 Start cycle**: Begin your pills on the 5th day after your period starts, counting the day that the bleeding starts as day 1 (even if it's 10 p.m. or later).
  The advantage to the **Sunday Start cycle** is that you will never have your period on the weekend. If this is important to you, use the **Sunday Start.**
  The advantage to the **Day 1 start cycle** is that you will be immediately protected from pregnancy. If maximizing the contraceptive effect of the "pill" is most important to you, use the **Day 1 Start**. There is no particular advantage to the **Day 5 Start** cycle.

Absolute contraindications: (your role as a doctor is to identify absolute from relative contraindications)

- Active thromboembolic disease
- Undiagnosed vaginal bleeding
- Acute or chronic obstructive liver disease
- Known or suspected breast cancer
- Known or suspected pregnancy
- Complex migraine

Precautions:

Hypertension	can use Ocs if hypertension controlled monitor the blood pressure if there is family history.
CVD, hyperlipidemia	OCs with new progestins preferred because of more favorable lipid profile
Diabetes	low dose OCs unlikely to affect glucose control but estrogen may complicate vascular disease
Epilepsy	some anticonvulsants ↓ OCs efficacy due to ↑ metabolism; may require use of OCs with >35ug EE
Hepatitis, cirrhosis	avoid OCs if active disease; may use if liver enzymes have returned to normal
Gallbladder disease	may be exacerbated by OCs
Migraine	avoid OCs if classic or complex (↑ risk of stroke)
Inflammatory bowel disease	active diarrhea may reduce absorption and efficacy of OCs and require backup method
Systemic lupus erythematosus	avoid OCs as estrogens can complicate vascular disease
Smoking women > 35	if light smoker (<15 cig/day) or on nicotine patch, can use 20 ug EE product with caution

Educate: you are a smoker & that will increase your risk of cardiovascular events.

OCP effects on other diseases:

OCs may exacerbate certain disease states:

- **Cholelithiasis** => due to increased cholic acid secretion and greater gallstone formation
- **Diabetes** => due to peripheral insulin resistance and impaired glucose metabolism
- **Hypertension** => due to sodium and water retention and increased renin activity
- **Hyperlipidemia** => due to increased triglycerides related to estrogen content and reduced HDL due to the effect of the progestin; although OCs containing the new progestins have the most favorable lipid profile, today's low dose OCs are all considered antiatherogenic.

OCs Early Danger Signs

Sign	Problem
Abdominal pain (severe)	Gallbladder disease, Pancreatitis, Hepatic adenoma, Thrombosis
Chest pain (severe), SOB	Pulmonary, embolus, Acute MI
Headaches (severe)	Stroke, Hypertension, Migraine
Eye problems “blurred vision, flashing lights, blindness”	Stroke, Hypertension, Vascular insufficiency
Severe leg pain	Deep vein thrombosis (DVT)

Benefits:

- **Simple and highly effective**
- **Reduces need for sterilization & abortion**
- **Significantly improves menstrual symptoms & regularity**
  - Reduces dysmenorrhea and mittelschmerz
  - Reduces menstrual blood loss (up to 50%)
  - Reduces risk of anemia
  - Reduces PMS
  - Alleviates menorrhagia/hot flashes in perimenopausal
- **Decreases incidence of disease**
  - bacterial pelvic inflammatory disease (60%)
  - ectopic pregnancy
  - Endometriosis
  - Endometrial cancer (>50%)
  - Ovarian cancer (>40%)
  - ovarian cysts (>60%)
  - acne and hirsutism
  - fibrocystic breast disease (50-75%)
  - Osteoporosis
  - rheumatoid arthritis (50%)

benefit greatest with long term use (>5yr) and persists up to 15 yrs after discontinuing

Risks:

Venous thromboembolism	- ↑ 3-4x with low dose OCs - further ↑ 2x with new progestins (estrogens ↓ activation of Protein C so ↑ risk of thrombus)
arterial thrombosis (MI, stroke)	- related to estrogen, age >35, smoking, hypertension, and other risk factors for CVD (↑~2-3x) - No ↑ risk over baseline in young non-smoking
Breast cancer	↑ 1.5x ; women who started OCs at early age, persists for 10yrs after d/c , nulliparity, delay in childbearing
Cervical cancer	↑ 1.5x with long term use (>5yr), early sexual activity, multiple partners
Gallbladder disease	↑ 1.5x during 1st 5yrs of OC use
may exacerbate and/or precipitate	hypertension, diabetes, gallbladder and liver disease, SLE, migraine headaches, depression, GERD, vaginal yeast infections
Other	does not protect against STDs

- New progestins may produce beneficial changes in the lipid profile compared to previous progestins, this may not be of great advantage.
- Cardiovascular events in OC users are thrombotic not athero-schlerotic in origin
- Women using nicotine gum or patches or those exposed to secondhand smoke have the same risk as those who actually smoke.

Side Effects and Their Management

1. **Breakthrough bleeding**
   - most common in 1st 3 months
   - if persists beyond 3-6 mon check for other causes (eg. chlamydia).
   - Change to OC with ↑ estrogen/progestin depending on when BTB occurs in the cycle
   - may also be related to poor compliance, smoking, DIs

Because the lower doses of estrogen in OCPs are insufficient to sustain endometrial integrity

2. **Breast tenderness**
   - if persists beyond 1st 3 months rule out pathologic causes
   - change to OC with ↓ estrogen/progestin

3. **Weight gain**
   - may cause ↑ appetite in 1st month but overall weight gain is minimal with low dose OCs and within normal limits for age related gain
   - may be cyclical due to Na & H2O retention

4. **Nausea**
   - often subsides within 3 months
   - take at hs with food or change to lower estrogen content

5. **Headache**
   - tension headaches unaffected but hormone related or vascular migraines may ↑↓; if precipitated or exacerbated by OCs should avoid their use

6. **Acne**
   - sometimes worsens initially but usually improves in the long term
   - change to ↓ androgenic OC or use topical therapy

7. **Chloasma**
   - irreversible and idiosyncratic
   - exacerbated by sunlight so use sunscreen and reduce exposure
   - ↓ estrogen dose

Drug interactions:

AGENT	EFFECT AND MECHANISM	MANAGEMENT
***Anticonvulsants:** Carbamazepine Ethosuximide Barbiturates Primidone Phenytoin	↓ OCs efficacy due to ↑ hepatic metabolism ↑ phenytoin conc. due to ↓ metabolism	Use OCs with 50 ug EE Change to alternate anticonvulsant Use alternate method of birth control (BC) Monitor serum phenytoin and ↓ dose prn
***Antibiotics:** Penicillins (esp.ampi) Cephalosporins Macrolides Metronidazole Sulfas/Cotrimoxazole Tetracycline **Rifampin**	↓ OCs efficacy due to ↑ intestinal transport (diarrhea) and ↓ enterohepatic reabsorption of estrogen ♦interaction with rifampin most significant! ↓ OCs efficacy due to ↑ metabolism	Estimated failure rate is approximately 1% per year Likely subgroup at ↑ risk due to dependence on enterohepatic reabsorption but unable to identify these ♀ so counsel all If long term treatment, use alternate method of BC; if short term, use back-up method of BC for that cycle Management as above for either long-term or short term
Antifungals: *Griseofulvin	↓ OCs efficacy due to ↑ metabolism	Management as above
Benzodiazepines: Alprazolam, Chlordiazepoxide, Diazepam, Nitrazepam, Triazolam Oxazepam, Lorazepam, Temazepam	↑ benzodiazepine conc. due to ↓ oxidative metabolism ↓ benzodiazepine conc. due to ↑ glucuronidative metabolism	Monitor for ↑ side effects and possible toxicity; reduce dose prn Monitor for loss of benzodiazepine effect and ↑ dose if needed
***Corticosteroids**	↑ steroid conc. due to ↓ metabolism	Monitor for side effects and toxicity; reduce dose as needed
***Cyclosporin**	↑ cyclosporin conc. due to ↓ metabolism	Monitor for side effects and toxicity and reduce dose as needed
Grapefruit juice	↑ estrogen levels due to ↓ metabolism	Monitor for side effects and switch to lower dose EE if needed May consider avoiding grapefruit juice; orange juice OK
Insulin and Hypoglycemics	OCs with 50 ug EE may impair glucose tolerance in predisposed women	Use OCs with 35 ug or less EE; monitor blood sugars and ↑ dose of insulin or hypoglycemic; Use alternate method of BC
Imipramine **Clomipramine**	↑ TCA conc. due to ↓ metabolism	Monitor for side effects and toxicity and reduce dose prn
Theophylline	OCs with ≥ 35 ug EE may ↑ theophylline conc. due to ↓ metabolism	Monitor theophylline levels and reduce dose prn Use OCs with < 35 ug EE
Thyroid	↓ levels of free thyroxine due to estrogen - induced ↑ in thyroxine binding globulin	May need to ↑ dose
***Warfarin**	OCs ↑ risk of thromboembolism and may ↑↓ anticoagulant effect due to changes in metabolism	Avoid OCs and use alternate method of contraception Monitor PT times and adjust dose esp. if OCs started, stopped, or changed (brand, dose, etc)

* of greatest clinical significance; (probably <5% of drug interactions with OCs results in pregnancy[29])

Management of missed dose:

- **#1 compliance problem especially if no set routine so should try to associate with some activity of daily living (eg. hs)**
- **risk of pregnancy greatest if pills started late or missed at the beginning or very end of a cycle**
- **a single missed dose of little consequence if remembered within the window of opportunity (12-24 hrs after last dose)**
- **CHECK WITH PHYSICIAN IF 2 MENSTRUAL PERIODS ARE MISSED IN A ROW**

SOGC Guidelines (for 21 day pill packs)[2]	International Planned Parenthood Federation Guidelines: (for 21-day pill packs)[19]
Miss 1 pill: Take it now and take subsequent pills as usual **Miss 2 pills in a row:** ◆**1st 2 weeks:** Take 2 pills now and 2 pills the next day Take subsequent pills as usual Use backup method for the 7 days following missed pills ◆ **3rd week*:** Discard remainder of pill pack and start new pack that same day Use backup method for the next 7 days **May not have a period this month** **Miss 3 pills in a row*:** Discard remainder of pill pack and start new pack that same day; Use backup method for the next 7 days **May not have a period this month** *** Sunday starters should continue taking 1 pill daily until Sunday and then follow instructions as above**	**How long since last pill taken??** **12 hours or less:** Take missed pill now Take subsequent pills as usual **More than 12 hours:** Take missed pill now Discard any other missed pills Use backup method for next 7 days **If >7 pills left**, finish package as usual and start new one 7 days later as usual **If < 7 pills left**, finish package as usual but start a new one the next day (no pill free break) - **may not have a period this month**

PROGESTIN ONLY PRODUCTS

The Progestin-only-pill (POP) "mini pill"

- indicated for use in women in whom estrogen is contraindicated or intolerable (eg. history of VTE or migraine, are postpartum or lactating, or who smoke)
- **contraindications:**
  - Pregnancy
  - Undiagnosed vaginal bleeding.
- Micronor (norethindrone) is the only POP currently available in Canada.
- The POP inhibits ovulation in only 60% of women so relies on endometrial and cervical mucus changes for its contraceptive effect. Compared to COCs, efficacy is somewhat lower at 90-99%.
- Cervical permeability diminishes within 22 hrs of ingestion and is unimpaired by 24hrs. Hence compliance is more critical as the **pills must be taken at the same time each day within 3 hrs for reliable effect.**

- POP should be started on **day 1** of the menstrual cycle and continued **daily** with no pill-free days.
- A backup method of contraception is required for the **first month**.
- If a pill is missed or delayed, it should be taken immediately and a backup method used for the next 48 hrs
- if 2 pills are missed, 2 pills should be taken stat, followed by 2 the next day and a backup method used till the next menstrual period.
- If no period occurs within 45 days, test for pregnancy.
- Due to the absence of estrogen and the reduced progestin content, side effects with POP are substantially reduced.
- Menstrual disturbances are the most common problem and patients should be so advised.
- Persistent abnormal bleeding should be investigated to rule out pathological causes
- If prolonged amenorrhea occurs, pregnancy status should be evaluated. Ovarian cysts and ectopic pregnancy may also occur infrequently.

Long-acting Progesterone depot injection (Depo-Provera)

- is a simple, well-tolerated and extremely reliable method with a failure rate of < 0.3% .2
- The sustained levels of medroxyprogesterone (MPA) suppress ovulation, induce endometrial atrophy and make cervical mucus impermeable to sperm.
- The **initial dose** should be injected in the **first 5 days** of the menstrual cycle to avoid inadvertent administration during early pregnancy.
- Appointments for **repeat injections** should be made at ~12 week
- dose is effective for up to 14 weeks
- If repeat injection is late, one must test to ensure that the patient is not pregnant prior to giving the next injection.

- **Indications:**
  - similar to POP but not exclusive of women simply desiring this method for convenience
- **Contraindications:**
  - pregnancy
  - Undiagnosed vaginal bleeding.
- **Advantages**:
  - scanty menses or amenorrhea (50% of women after 1yr)
  - prevention of anemia
  - reduction in PMS, dysmenorrhea, endometriosis
  - less pelvic inflammatory disease
  - reduced risk of endometrial and cervical cancers
  - reduced seizure frequency
- **Drawbacks:**
  - menstrual cycle disturbance
  - weight gain of an average of 1-2 kg/yr (reversible)
  - decreased bone density related to dose and duration (reversible)
  - delay in return of ovulation (average = 8 months but may take up to 2yrs)
  - headache, mood changes, lethargy, mastalgia, bloating, acne

Progestin Implant (Norplant)

- provides the most effective method of hormonal contraception with a failure rate of <0.2%.2
- Unlike depot injections, problems with patient compliance are eliminated once the device is inserted
- reliable contraception is provided for up to **5 years**.
- **Indications and contraindication** are similar to the other progestin-only products.

- Inserted subdermally on the medial aspect of the upper arm. slowly release the levonorgestrel which inhibits ovulation, induces endometrial atrophy, and makes cervical mucus impermeable to sperm
- The device should be inserted within the **first few days** of the menstrual cycle and is effective within 24hrs.
- **Disadvantages**:
  - high cost
  - need for surgical insertion and removal
  - menstrual cycle disturbance
  - weight gain
  - reductions in HDL
  - ovarian cysts
  - headache, depression, mastalgia, acne

The "Morning After Pill" (MAP)

- The MAP provides emergency post-coital contraception (EPC) when given **within 72 hrs** of unprotected intercourse occurring around the time of ovulation.
- The probability of pregnancy approaches zero if intercourse occurs more than 2 days after ovulation.
- For maximum efficacy, MAP should be given within 72 hrs after unprotected sex, and ideally within the first 24 hrs. After 72 hrs the efficacy of MAP rapidly declines and it is **ineffective by 7 days**. This method (Yuzpe) results in a 75% reduction in the number of pregnancies that would occur if no EPC were used.
- **Ovral** is considered the pill of choice because of its low failure rate (<2%) and reduced risk of nausea and vomiting.
- pills are taken immediately followed by 2 pills 12 hrs later; alternately 2 pills OD x 2 days can be given particularly if pills would otherwise have to be taken in the evening or night hours or when nausea with vomiting is likely.

- MAP **failure rates range from 0-2.4%** (i.e. 98% of women will menstruate within 21 days)
- **side effects:**
  - Nausea and vomiting "**Doses vomited within 1 hr of ingestion must be repeated.** Prophylactic antiemetics can be given prophylactically with each dose (eg. dimenhydrinate)"
  - Cramping
  - Spotting
  - Breast tenderness
- **Follow-up:**
  - Patients should be seen 1 week later for and again in 3-6wks; if little or no bleeding occurs after 21 days, a pregnancy test should be done.
- Patients should be advised to contact their doctor if they have severe abdominal pain, chest pain, headache, eye problems or leg pain.

Take home messages:

- Switching the OCs within the first 3 months is usually not necessary due to the self-limiting nature of many initial symptoms.
- Compliance and overall efficacy can be enhanced by providing adequate instruction on the importance of establishing a regular pill-taking routine, proper initiation of OCs, managing missed doses, occurrence and management of common side effects, early danger signs, and the possibility and management of drug interactions including use of backup methods of contraception.
- Current low dose OCs are highly effective with an excellent safety profile and many associated health benefits
- No single product has been shown to be superior in efficacy, safety or tolerability
- There is no "one size fits all" OC; different women may require different formulations
- Smoking particularly after age 35 with concurrent OC use greatly increases cardiovascular and thrombotic risks
- Age alone is not a significant risk and OCs are considered safe for use in women up to the age of menopause

Notes on other forms of contraception:

- Anything inserted vaginally (vaginal rings/ IUD) are not options in a patient who's never been married.
- Injectible is also hormonal but the difference from OCP is the return to fertility, so it is an option but the risk of thrombosis/ cardiovascular events is similar to OCP.
- Injectable has an unpredictable return to fertility. OCP can return to normal fertility in 1 month.
- Condoms are a good option however patients in our community probably don't have risk of STI.
- Condoms protective value is 80%-87%
- OCP protective value is ~98%
- How to advice patients to use condoms properly? No intercourse before ejaculation without wearing it. Penetration without ejaculation is not fine! Pre-ejaculate fluid can have sperm.
- Lubricant has to be water based, avoid silicon/ oil based. They break the condom.
- How to decide between condoms & OCP?
    - Patient's & husband preference, how big of a deal is it if she got pregnant? If big deal go with OCP.
- History of DVT is very important in prescribing OCP. There is risk of recurrent DCT so you would do coagulation profile.

2-Menopause

Definition :

Menopause is the physiologic transition when the ovaries stop releasing eggs, ovarian function decrease, and menstrual periods stop.

Symptoms:

Some women go through the menopausal transition without symptoms, many women have **hot flashes** or **genital tract symptoms**, such as vulvar or vaginal **dryness**, **painful intercourse**, and **urinary problems.**

- When counseling patients who are going through menopause, clinicians should understand the benefits and risks of hormone therapy, non-hormonal prescription medications , and alternative treatments, and be familiar with various delivery methods

Risks and Benefits of Hormone Therapy

2002 WHI trial	Combined regimen increased the risk of **coronary artery disease**, **breast cancer**, **stroke**, and **venous thromboembolism** , **decreased** risk of **colorectal cancer**, h**ip fractures,** and **total fracture**
2004 WHI trial	Conjugated **estrogen–only** in women without a uterus, taking estrogen alone had **no significant change** in risk of coronary heart disease or breast cancer and,similar to the trial of combined estrogen and progestogen, an **increase in strokes and VTE**
2014	Women taking **estrogen alone** had a significantly **reduced risk of breast cancer.**

- Starting HT early (compared with 10 years after menopause) may be cardioprotective because of estrogen slow the progression of atherosclerosis in younger women.
- Current guidelines recommend against using hormone therapy to prevent or treat **cardiac disease.**
- The American Academy of Family Physicians recommends against using HT for the prevention of **chronic conditions**.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Combined estrogen/progestogen therapy, but not estrogen alone, increases the risk of breast cancer after three to five years of use.	B	3
Systemic estrogen, alone or in combination with a progestogen, is the most effective therapy for menopausal hot flashes, and is approved by the U.S. Food and Drug Administration for this indication.	A	9
Because of the potential risks with long-term use of hormone therapy, clinicians should prescribe the lowest effective dosage for the shortest duration necessary to improve symptoms.	C	8, 12
There is no high-quality, consistent evidence that black cohosh, botanical products, omega-3 fatty acid supplements, or lifestyle modification alleviates hot flashes.	B	19-21
The decision to continue combined hormone therapy for more than three to five years should be made after reviewing the risks, benefits, and symptoms with the patient.	C	12
Effective nonhormonal therapies for genitourinary syndrome of menopause include vaginal moisturizers and oral ospemifene (Osphena).	B	31, 32

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.

Vasomotor Symptoms

- Vasomotor symptoms (hot flashes) are **the most common indication** for hormone therapy
- During menopause, approximately 70% of women report hot flashes, which are more common in women with a higher body mass index, with lower income and education, who smoke cigarettes, or who are black.
- Treatment options include hormone therapy, non-hormonal prescription medications, and clinical hypnosis.
- **Estrogen** is the **most effective** therapy for hot flashes and is approved by the U.S. (FDA) for this indication.
- Although some women may prefer lifestyle modification, there is no evidence that lowering the ambient temperature; using fans; exercising; or avoiding triggers, such as alcohol and spicy foods, improves hot flashes.
- All systemic estrogen formulations are effective, patient preference should guide the choice of therapy, unless there are **contraindications** such as undiagnosed vaginal bleeding or a history of breast cancer, VTE, or severe liver disease.

Table 1. Estrogen Medications for the Treatment of Vasomotor Symptoms

Medication	*Available dosages (mg)*	*Bioidentical?*	*Cost**
Oral			
Enjuvia (conjugated estrogen)	0.3, 0.45, 0.625, 0.9, 1.25 (per day)	No	$87
Estrace (estradiol)	0.5, 1.0, 2.0 (per day)	Yes	$131
Menest (esterified estrogen)	0.3, 0.625, 1.25, 2.5 (per day)	No	$48
Premarin (conjugated estrogen)	0.3, 0.45, 0.625, 0.9, 1.25 (per day)	No	$143
Transdermal patch (estradiol)			
Alora	0.025, 0.05, 0.075, 0.1 (twice per week)	Yes	$90
Climara	0.025, 0.0375, 0.05, 0.06, 0.075, 0.1 (once per week)	Yes	$50
Minivelle	0.025, 0.0375, 0.05, 0.075, 0.1 (twice per week)	Yes	$137
Vivelle Dot	0.025, 0.0375, 0.05, 0.075, 0.1 (twice per week)	Yes	$84
Transdermal gel (estradiol)			
Divigel	0.25, 0.5, 1.0 (per day)	Yes	$118
Elestrin	0.52 (per day; adjust dosage based on response)	Yes	$109
Estrogel	0.75 (per day)	Yes	$126
Transdermal spray (estradiol)			
Evamist	1.53 per spray (start with 1 spray per day, adjust up to 3 sprays per day based on response)	Yes	$118
Vaginal (estradiol)			
Femring	0.05, 0.10 (for 90 days)	Yes	$355

**—Estimated retail price of one month's treatment based on information obtained at http://www.goodrx.com (accessed June 13, 2016).*

Vasomotor Symptoms:Cont

- **No** studies have shown that **transdermal estrogen** may have a lower risk of VTE .
- All estrogen medications should be given at the **lowest** effective dosage for the **shortest** duration
- If necessary, the dosage may be increased after evaluating for effectiveness during the first eight weeks of therapy, with reassessment annually or as needed.
- Because all formulations of unopposed estrogen increase the risk of **endometrial hyperplasia** and cancer in women with a uterus, these patients should use **estrogen plus progesterone** for endometrial protection; a continuous regimen is more effective than sequential therapy .
- Patients can take an estrogen/progestogen combination product *(Table 2)* or an estrogen product used in conjunction with a separate progestogen.
- Progestogens can cause fatigue, dysphoria, and fluid retention
- Patients with a uterus who cannot tolerate these adverse effects may benefit from **Duavee**, a combination of 0.45-mg conjugated equine estrogen and the selective estrogen receptor modulator **bazedoxifene**, which is approved by the FDA for treating hot flashes and preventing osteoporosis.
- **Bazedoxifene** does not stimulate the endometrium. **Duavee** is contraindicated in women who have a history of breast cancer or VTE.
- The levonorgestrel- releasing intrauterine system (Mirena) is an off-label option for providing local progestogen to the endometrium for patients who cannot tolerate systemic therapy.

Table 2. Combination Estrogen/Progestogen Medications for the Treatment of Vasomotor Symptoms

Medication	*Available dosages (mg of estrogen/progestogen unless otherwise indicated)*	*Cost**
Oral		
Activella (estradiol/norethindrone acetate)	0.5/0.1, 1.0/0.5 (per day)	$215
Angeliq (estradiol/drospirenone)	0.5/0.25, 1.0/0.5 (per day)	$133
Duavee (conjugated equine estrogen/bazedoxifene)	0.45/20.0 (per day)	$153
Femhrt (estradiol/norethindrone acetate)	2.5 mcg/0.5 mg (per day)	$150
Prefest (estradiol/norgestimate)	1.0/0.09 (per day; estrogen alone for 3 days followed by estrogen/progestogen for three days, then repeat)	$120
Premphase (conjugated estrogen/ medroxyprogesterone)	0.625/5.0 (per day; estrogen alone for days 1 to 14 then add progestogen for days 15 to 28)	$161
Prempro (conjugated estrogen/medroxyprogesterone)	0.3/1.5, 0.45/1.5, 0.625/2.5, 0.625/5.0 (per day)	$161
Transdermal patch		
Climara Pro (estradiol/levonorgestrel)	0.45/0.015 (once per week)	$149
Combipatch (estradiol/norethindrone acetate)	0.05/0.14, 0.05/0.25 (twice per week)	$158

NOTE: *None of these therapies are bioidentical.*

**—Estimated retail price of one month's treatment based on information obtained at http://www.goodrx.com (accessed June 13, 2016).*

Despite the effectiveness of estrogen, some patients may prefer non-hormonal medications or may have contraindications to using estrogen.

Several antidepressants reduce hot flashes*(Table 3)*.

Table 3. Antidepressants for Nonhormonal Treatment of Vasomotor Symptoms

Antidepressant	*Dosage (mg per day)*	*Cost**
Citalopram (Celexa)	10 to 20	$10 ($231)
Clonidine (Catapres)	0.1	$9 ($79)
Desvenlafaxine (Khedezla)	100 to 150	$257 ($384)
Escitalopram (Lexapro)	10 to 20	$13 ($256)
Gabapentin (Neurontin)	900 to 2,400	$14 ($340)
Paroxetine salt (Brisdelle)	7.5	NA ($190)
Paroxetine (Paxil)	10 to 25	$10 ($178)
Pregabalin (Lyrica)	150 to 300	NA ($185)
Venlafaxine (Effexor XR)	37.5 to 100	$17 ($300)

NA = not available.

**—Estimated retail price of one month's treatment based on information obtained at http://www.goodrx.com (accessed June 13, 2016). Generic price listed first; brand price listed in parentheses.*

Clonidine adverse events, such as hypotension, dizziness, and rebound hypertension, limit its usefulness for menopausal symptoms.

Low-dose paroxetine (Brisdelle)

- The only non-hormonal medication approved by the FDA to treat hot flashes, other dosages can be used.
- Shouldn't be used with tamoxifen because of ↓Cytochrome P450 2D6, which ↓the effectiveness of tamoxifen.

Desvenlafaxine (Khedezla) and venlafaxine

- Do not inhibit CYP2D6 and are appropriate alternatives.
- Starting at a low dose and titrating should be considered for antidepressants other than paroxetine.

Other non-hormonal options include gabapentin (Neurontin) and pregabalin (Lyrica).

- These medications can cause dizziness and other adverse effects, and should be titrated from a lower dosage.

Stellate ganglion block of the C6-T2 anterior cervical spine has shown promise

Vasomotor Symptoms:Cont

- Some patients may want to use alternative therapies or compounded formulations.
- Clinicians should counsel patients that there is no high-quality, consistent evidence that black cohosh, many botanical products, and omega-3 fatty acid supplements are effective for treating hot flashes.
- Soy-based foods and supplements have a modest benefit in reducing hot flashes and vaginal dryness
- Red clover and some non-Chinese herbal medicines variably improved symptoms.
- Plant-based complementary therapies. Yoga, paced respiration, acupuncture, exercise, stress reduction, and relaxation therapy have not been proven to alleviate hot flashes. However, clinical hypnosis (five 45-minute sessions weekly) has been shown to reduce hot flashes by 74%, compared with a 17% reduction in patients who received only education and encouragement
- Bioidentical hormones, such as estrone, 17-beta estradiol, and estriol, are identical to human hormones. Data are limited about the safety and effectiveness of compounded bioidentical formulations. There is concern that these unregulated formulations may have similar adverse effects as estrogen medications, such as endometrial hyperplasia.
- If a patient prefers a bioidentical hormone, FDA-approved medications containing the bioidentical hormone estradiol can be considered; for women with a uterus, micronized progesterone (100 mg or 200 mg per day) should be added.

Deciding When to Discontinue Hormone Therapy

- Because of the potential increased risk of breast cancer in women taking combined estrogen/progestogen therapy, some clinicians advise that patients discontinue therapy after three to five years.
- An analysis of women in the WHI combined hormone trial who had hot flashes when starting therapy showed that after discontinuation, 56% had moderate to severe hot flashes compared with 21% of women who took placebo.
- Clinicians should inform patients that some women will have a difficult time stopping hormone therapy. Some patients will be successful with abrupt discontinuation, whereas others may benefit from weaning.
- The American College of Obstetricians and Gynecologists recommends against routine discontinuation based on age or treatment duration, and advises that the decision to continue or stop hormone therapy should be individualized based on the patient's symptoms and medical history.

Transitioning from Contraception to Hormone Therapy

- Transitioning from contraception to hormone therapy may be challenging because oral contraceptives have higher dosages than typical hormone therapy regimens.
- measuring follicle-stimulating hormone levels after stopping oral contraceptives can be inaccurate during perimenopause.
- Rise in follicle-stimulating hormone level without a change in estradiol levels two weeks after stopping oral contraceptives is evidence that it is safe to transition to hormone therapy.
- Others suggest discontinuation of contraception when women are in their mid-50s because spontaneous conception is rare at this age.

Genitourinary Syndrome of Menopause

Genitourinary syndrome of menopause refers to bothersome genital symptoms from changes in the vulva, vagina, and lower genital tract that are caused by diminished estrogen. It replaces the terms vulvovaginal atrophy and atrophic vaginitis

Several changes to genital anatomy due to decreased estrogen

- Thinning of the vulvar mucosa may cause vulvar burning, irritation, or constriction of the introitus, resulting in entry dyspareunia
- Narrowing of the vagina and decreased lubrication can cause painful intercourse or coital bleeding
- Diminished estrogen may also lead to recurrent urinary tract infections and urinary urgency

Genitourinary syndrome of menopause is often progressive without treatment.

- Women using low-dose vaginal estrogen for less than one year should not require a progestogen to decrease the risk of endometrial cancer.
- Clinicians should consider an endometrial biopsy and/or transvaginal ultrasonography if spotting or bleeding occurs while using low-dose vaginal estrogen.
- The decision to use vaginal estrogen formulations for women with a history of hormone-dependent cancers should be based on the woman's preference after consultation with a clinician experienced with hormone therapy.
- Clinicians can inform patients that there is no evidence that using low-dose local estrogen increases the risk of breast cancer recurrence.
- Topical estrogen for vaginal symptoms (dryness) **has to be local.** Even if she is already taking systematic.
- Other benefits of local estrogen: protect from UTI & Stress/urge incontinence.
- Local estrogen is very important for sexually active patients for comfortable enjoyable sex.

Genitourinary Syndrome of Menopause:Cont

- It is reasonable to try nonhormonal therapy as a first-line option to alleviate vulvovaginal symptoms caused by genitourinary syndrome of menopause. Although not as effective as estrogen
- Vaginal moisturizers, such as Replens, are an effective treatment for mild vaginal dryness and related dyspareunia.
- Ospemifene is the only FDA-approved nonhormonal therapy for dyspareunia caused by menopausal atrophy. ospemifene improve vaginal dryness. It should not be used by women with a history of breast cancer or thromboembolic disease. Hot flashes are the most bothersome adverse effect.
- Patients does not respond to non-hormonal medications or who have a narrow introitus or vagina may benefit from low-dose vaginal estrogen.
- All estrogen formulations for genital atrophy appear to have similar effectiveness regardless of administration method.Patient preference should guide the choice of formulation.
- Creams have the advantage of both intravaginal and vulvar application, but they can be messy to apply.
- Some patients may prefer the convenience of vaginal estradiol tablets (Vagifem) or the vaginal low-dose estradiol ring (Estring), which provides three months of continuous therapy. Femring, another vaginal ring, provides a systemic dosage of estrogen for treating hot flashes.

Table 4. Treatment Options for Genitourinary Syndrome of Menopause

Treatment	*Dosages*
Estrace vaginal cream (estradiol) 0.01%	Usual dosage: 2 to 4 g applied daily for one to two weeks, then 1 g applied one to three times per week for maintenance therapy
Estring (estradiol) vaginal ring	2 mg released at 7.5 mcg per day over three months
Osphena (ospemifene)	60 mg per day taken orally with food
Premarin (conjugated estrogen) vaginal cream	0.625 mg of conjugated equine estrogen per g; usual dosage: 0.5 to 2 g applied daily for 21 days then off for seven days, or more commonly one to three times per week for maintenance therapy
Replens vaginal moisturizer	Applied three times per week
Vagifem (estradiol) vaginal tablet	10 mcg applied once daily for two weeks, then twice weekly

Menopause Quick 6 (MQ6)

6-question scale assesses menopausal symptoms for which there are evidence-based treatment options while providing a patient-centred assessment to guide treatment choices.

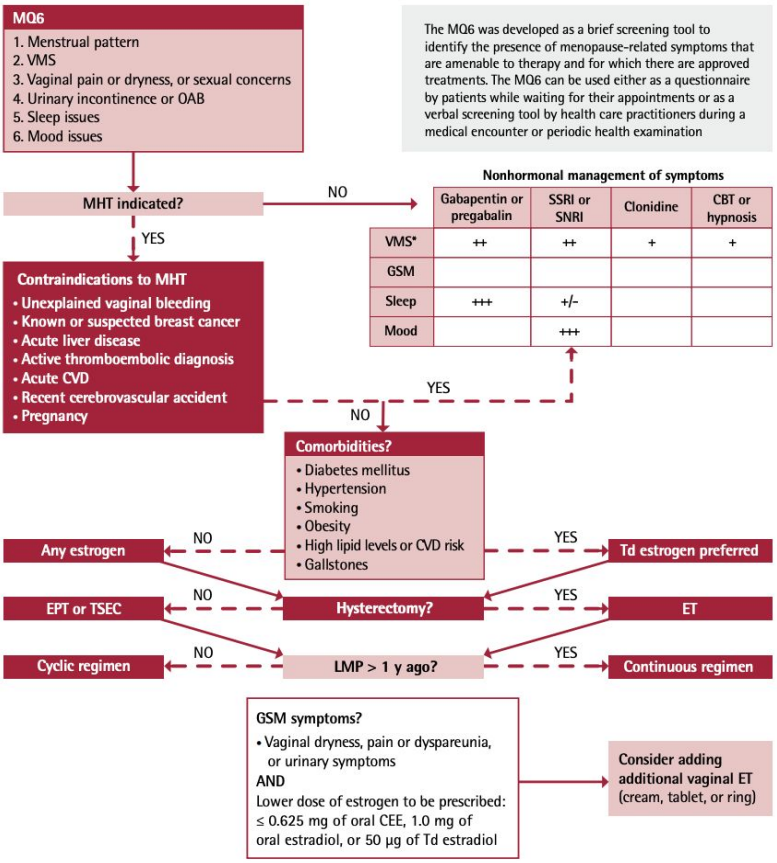
Table 1. How to use the information elicited by questions that comprise the Menopause Quick 6

QUESTION	INTERPRETATION
Q1: Any changes in your periods?	Menstrual irregularities signal imminent menopause. A recent study found that when VMS start before the cessation of menses, they can be expected to last longer (median 11.8 y) than VMS that start after the LMP (3.4 y).[10] Further, when prescribing MHT for women who are still cycling irregularly or within 1 y of their LMP, a cyclic hormone regimen should be used.[11] If the LMP was more than 1 y ago, continuous regimens can be offered. For all women with cessation of menses younger than 45 y, MHT is recommended
Q2: Are you having any hot flashes?	Up to 80% of menopausal women experience VMS. When these are mild, many lifestyle and nonhormonal interventions can be effective. Moderate to severe VMS are treated most effectively by hormone therapy[4,6]
Q3: Any vaginal dryness or pain, or any sexual concerns? Q4: Any bladder issues or incontinence?	The term *vulvovaginal atrophy* has been replaced by *genitourinary syndrome of menopause*, reflecting the changes to the vulva, vagina, and urinary tract and to sexual functioning owing to the menopausal drop in estrogen. Many women are reluctant to talk about their vaginal or sexual concerns, bladder issues, or incontinence, yet these can have a substantial negative effect on quality of life. We have effective treatments for these symptoms, so we must ask
Q5: How is your sleep?	Sleep disturbances are common during menopause and are most often attributed to hot flashes.[2] Poor sleep can exacerbate mood and anxiety issues and contribute to cognitive complaints and even weight gain
Q6: How is your mood?	Menopause is a high-risk time for first-episode or recurrent depression.[12] In addition, anxiety and irritability peak during perimenopause. Both SSRIs and SNRIs have been shown to be effective for these mood disorders while having a beneficial effect on VMS. Women who remain symptomatic despite these medications might benefit from hormonal augmentation

LMP—last menstrual period, MHT—menopausal hormone therapy, SNRI—serotonin-norepinephrine reuptake inhibitor, SSRI—selective serotonin reuptake inhibitor, VMS—vasomotor symptoms.

New guidelines have been created, with the consensus that MHT is safest for those younger than 60 years and within 10 years of menopause and might be continued for some women after age 65

Figure 2. Evidence-based algorithm for management of menopausal symptoms



CBT—cognitive-behavioural therapy, CEE—conjugated equine estrogen, CVD—cardiovascular disease, EPT—estrogen-progestogen therapy, ET—estrogen therapy, GSM—genitourinary syndrome of menopause, LMP—last menstrual period, MHT—menopausal hormone therapy, MQ6—Menopause Quick 6, OAB—overactive bladder, SNRI—serotonin-norepinephrine reuptake inhibitor, SSRI—selective serotonin reuptake inhibitor, Td—transdermal, TSEC—tissue-selective estrogen complex, VMS—vasomotor symptoms.
*In this table, + indicates some evidence of efficacy, ++ indicates good evidence of efficacy, +++ indicates strong evidence of efficacy, and +/- suggests the treatment might improve or worsen symptoms. Data from the North American Menopause Society.[5]

- when hormone therapy is indicated and there are no contraindications to MHT, then a transdermal preparation, which avoids first-pass hepatic metabolism, is recommended for women with comorbidities that increase cardiovascular risk, including risk of venous thromboembolism or stroke.

- As the progestogen in the MHT regimen provides endometrial protection, patients who have undergone a hysterectomy require only estrogen therapy. When endometrial protection is required, the use of either estrogen-progestogen therapy or a tissue-selective estrogen complex is recommended.

- In the first year after menopause begins, women will often bleed when taking a continuous MHT regimen, so a cyclic regimen is preferred.
- Cyclic regimens usually include a steady dose of an estrogen for days 1 to 25 or 1 to 31 of the month, accompanied by a progestogen for 12 to 14 days of the month, resulting in withdrawal bleeding.
- Continuous regimens use steady daily doses of an estrogen and progestogen.
- Of note, we are now treating with lower-dose regimens of MHT, which do not always provide sufficient treatment of the local symptoms of GSM. For adequate treatment of local symptoms, **the addition of vaginal estrogen therapy should be considered.**

Symptoms of menopause:

- Increased libido happens around perimenopause because of the surge in estrogen, decreased libido happens after menopause.
- 12 Months with no period is menopause.
- 25% of bone density is built at puberty, equivalent to what's lost during menopause.

3-OSTEOPOROSIS

❖ Burden and care gaps

- ❖ **Osteoporosis is a silent disease till the patient gets fragility fractures**, the consequence of osteoporosis, are responsible for excess mortality, morbidity, chronic pain, admission to institutions and economic costs.
- ❖ Anything below two steps is minor trauma (fragility fracture)
- ❖ In KSA our range is 29%-36%, equivalent to the rest of the world. However our difference is that we start very early, at 40-80 years old.. While the screening in international recommendations is at 65 years old.
- ❖ They represent **80%** of all fractures in menopausal women **over age 50.**
- ❖ Those with **hip** or **vertebral** fractures have substantially increased risk of death after the fracture.
- ❖ Post-fracture mortality and institutionalization rates are higher for men than for women.
- ❖ fewer than 20% of women and 10% of men receive therapies to prevent further fractures. These statistics contrast sharply with the situation for cardiovascular disease, where 75% of patients who have had myocardial infarction receive β-blockers to prevent another event.

❖ Key points

- ❖ The management of osteoporosis should be guided by an assessment of the patient's absolute risk of osteoporosis- related fractures.
- ❖ Fragility fracture increases the risk of further fractures and should be considered in the assessment.
- ❖ Lifestyle modification and pharmacologic therapy should be individualized to enhance adherence to the treatment plan.

❖ Clinical recommendations

1- Who should I assess for osteoporosis and fracture risk?

- **Women** and **men** over age **50** should be assessed for risk factors for osteoporosis and fracture to identify those at high risk for fractures.
- Individuals over age 50 who have experienced a fragility fracture should be assessed [grade A].

❖ Cont: Clinical recommendations

2-How do I assess for osteoporosis and fracture risk?

A detailed history and a focused physical examination are recommended to identify risk factors for low bone mineral density, falls and fractures, as well as undiagnosed vertebral fractures.

In selected individuals, bone mineral density should be measured with dual-energy x-ray absorptiometry (Table 1).

1. Measure height annually, and assess for the presence of vertebral fractures [grade A].
2. Assess history of falls in the past year. If there has been such a fall, a multifactorial risk assessment should be conducted, including the ability to get out of a chair without using arms [grade A].

Table 1: Indications for measuring bone mineral density These change our minds of when to screen.

Older adults (age ≥ 50 yr)	Younger adults (age < 50 yr)
Age ≥ 65 yr (both women and men)	Fragility fracture
Clinical risk factors for fracture (menopausal women, men age 50–64 yr)	Prolonged use of glucocorticoids*
Fragility fracture after age 40 yr	Use of other high-risk medications†
Prolonged use of glucocorticoids* Give prophylactic bisphosphonates.	Hypogonadism or premature menopause (age < 45 yr)
Use of other high-risk medications†	Malabsorption syndrome
Parental hip fracture	Primary hyperparathyroidism
Vertebral fracture or osteopenia identified on radiography	Other disorders strongly associated with rapid bone loss and/or fracture
Current smoking	
High alcohol intake	
Low body weight (< 60 kg) or major weight loss (> 10% of body weight at age 25 yr)	
Rheumatoid arthritis	
Other disorders strongly associated with osteoporosis	

*At least three months cumulative therapy in the previous year at a prednisone-equivalent dose ≥ 7.5 mg daily.
†For example, aromatase inhibitors or androgen deprivation therapy.

If you have a patient whom you gave Vit D yet they didn't get better, screen for celiac.

What investigations should I order initially?

- For most patients with osteoporosis, defined as bone mineral density of **2.5 or more** standard deviations below the peak bone mass for young adults (i.e., T-score ≤ –2.5), only limited laboratory investigations are usually required (Box 1).

- Increased values for **bone turnover markers** are associated with an approximately two-fold increased risk of fractures,which is largely independent of bone mineral density

Cont: What investigations should I order initially?

Box 1: Recommended biochemical tests for patients being assessed for osteoporosis

- Calcium, corrected for albumin
- Complete blood count
- Creatinine
- Alkaline phosphatase
- Thyroid-stimulating hormone
- Serum protein electrophoresis (for patients with vertebral fractures)
- 25-Hydroxyvitamin D*

*Should be measured after three to four months of adequate supplementation and should not be repeated if an optimal level (at least 75 nmol/L) is achieved.

Perform **additional biochemical testing** to rule out secondary causes of osteoporosis in selected patients, on the basis of the clinical assessment [grade D].

Measure **25-hydroxyvitamin D** in those who will receive pharmacologic therapy for osteoporosis, who have sustained recurrent fractures ,bone loss despite treatment, those with comorbid conditions that affect absorption or action of vitamin D [grade D].

Serum 25-hydroxyvitamin D should be measured after **3-4** months of adequate supplementation and should not be repeated if an optimal level (**≥ 75 nmol/L**) is achieved [grade B].

Serum 25-hydroxyvitamin D should not be measured in healthy adults at low risk of vitamin D deficiency, i.e., without osteoporosis or conditions affecting the absorption or action of vitamin D [grade D].

- Vertebral fractures unrelated to trauma are best defined (on lateral radiographs or via vertebral fracture assessment)
- vertebral height loss of 25% or more with disruption of the end plate are associated with a 5 fold increase in the risk of future vertebral fractures relative to those without vertebral fractures.
- Perform lateral thoracic and lumbar spine radiography or vertebral fracture assessment by dual-energy x-ray absorptiometry if clinical evidence is suggestive of a vertebral fracture [grade A].

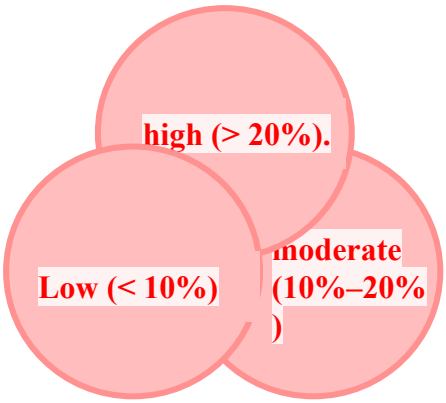
❖ How do I assess 10-year fracture risk?

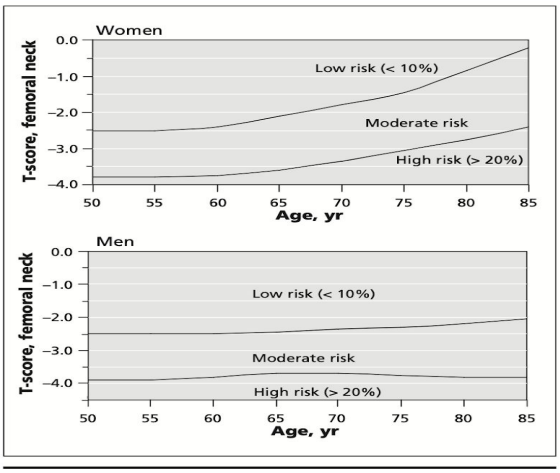
Currently, two tools are available for estimating the 10-year risk of a major osteoporotic fracture (i.e., fracture of the hip, vertebra [clinical], forearm or proximal humerus):

1. The updated tool of the **Canadian Association of Radiologists and Osteoporosis Canada**
2. The **Fracture Risk Assessment tool (FRAX)** of the World Health Organization (WHO

Both use the **bone mineral density or T-score for the femoral neck only.**

❖ CAROC tool stratifies women and men over age 50 into **three zones** of risk for major osteoporotic fracture within 10 years (Figure 1):





Hip fracture 10 year probability of fracture:
Low <3%
High >3% ❖ **clinical factors increase the risk of fracture**

Presence of a prior **fragility fracture after age 40**

\+

Recent prolonged use of systemic **glucocorticoid** at least 3 months use dose ≥ 7.5 mg daily

→

The presence of either risk factor raises the individual's risk to the next risk category (i.e from moderate to high). When both are present, the patient is considered to have a **high risk of fracture,** regardless of bone mineral density.

- CAROC initial risk category is obtained from age, sex and T-score for the femoral neck.
- The WHO Fracture Risk Assessment tool uses sex, age, body mass index, prior fracture, parental hip fracture, prolonged glucocorticoid use, rheumatoid arthritis (or secondary causes of osteoporosis), current smoking, alcohol intake (three or more units daily) and (optionally) bone mineral density of the femoral neck.

Cont: How do I assess 10-year fracture risk?

- Fracture discrimination using the WHO Fracture Risk Assessment tool with bone mineral density is **better** than the Fracture Risk Assessment tool without bone mineral density or bone mineral density alone.
- Bone mineral density of the **lumbar spine** is not considered in the initial risk assessment for either of these two tools, and fracture risk is slightly underestimated when the lumbar spine T-score is much lower than the hip T-score.
- Neither of these models should be applied to individuals **younger than age 50.** For individuals younger than age 50 with medical conditions that may have adverse skeletal consequences, risk assessment and treatment considerations are complex and often benefit from consultation with a specialist.
- The results obtained with these risk assessment tools reflect the theoretical risk of a patient who is treatment naive; they do not reflect any reduction in risk associated with therapy.
- for purposes of reporting **bone mineral density,** the 2010 version of the CAROC tool is the only system that can be applied.
- WHO Fracture Risk Assessment tool allows assessment of risk in the absence of a bone mineral density measurement and is more accurate for patients with one or more of the additional risk factors listed above.

Assessment of the absolute risk of fracture should be based on established factors, including age, bone mineral density, prior fragility fractures and glucocorticoid use [grade A].

For purposes of **reporting bone mineral density**, the 2010 version of CAROC tool is currently the preferred national risk assessment system [grade D].

Multiple fractures confer greater risk than a single fracture. In addition, prior fractures of the **hip** and **vertebra** carry greater risk than fractures at other sites [grade B].

Individuals with a T-score for the lumbar spine or total hip ≤ **–2.5** should be considered to have at least **moderate risk** [grade D].

Only the T-score for the **femoral neck** should be used to calculate risk of future osteoporotic fractures under either system [grade D].

❖ What are the therapeutic options?

1. Exercise and prevention of falls

- Exercise improves quality of life for those with osteoporosis, particularly physical function and pain, muscle strength and balance. There is limited evidence that exercise programs reduce fractures.

- Home safety assessment was effective only for those with severe visual impairment and others at high risk for falls.

1	**Exercises involving resistance training and/or weight-bearing aerobic like walking, jogging**	**recommended for those with osteoporosis or at risk for osteoporosis [grade B].**
2	**Exercises for core stability to compensate for weakness or postural abnormalities**	**Recommended for individuals who have had vertebral fractures [grade B]**
3	**Exercises that focus on balance (tai chi ,on balance and gait training)**	**should be considered for those at risk of falls [grade A].**
4	**Use of hip protectors**	**older adults in long-term care facilities who are at high risk for fracture [grade B].**

30-60 minutes walking a day is wonderful.

2- Calcium and vitamin D

Calcium And Vitamin D	The total daily intake of elemental calcium (through diet and supplements) for individuals over age 50 should be **1200 mg** [grade B].	For adults **>50** at moderate risk of vit D deficiency, supplementation with **800–1000 IU** (20–25 µg) vitD3 daily is recommended. To achieve optimal vit D status, daily supplementation > 1000 IU (25 µg) may be required. Daily doses up to 2000 IU (50 µg) are safe [grade C].
	For healthy adults ↓ risk of vitamin D deficiency, routine supplementation with **400–1000 IU (10–25 µg)** vitamin D3 daily is recommended [grade D].	For individuals receiving pharmacologic therapy for osteoporosis, measurement of serum vitamin D should follow 3-4 months of adequate supplementation and should not be repeated if an optimal level (≥ **75 nmol/L**) is achieved [grade D].

Pharmacologic therapy

- Pharmacotherapy reduces the risk of vertebral fracture by 30% to 70%, depending on the agent and level of adherence.
- Both calcitonin and teriparatide may decrease the pain associated with vertebral fractures.
- The potential benefits and risks of the prescribed agents should be discussed before therapy is initiated, to support informed decision-making

menopausal women requiring treatment of osteoporosis	prevention of **hip**, **nonvertebral** and **vertebral** fractures	alendronate, risedronate, zoledronic acid and denosumab can be used as **first-line therapies**
	prevention of **vertebral** fractures	- raloxifene can be used as a **first-line therapy** - intolerant of first-line therapies, calcitonin or etidronate can be considered
For menopausal women requiring treatment of osteoporosis + treatment for vasomotor symptoms	prevention of **hip**, **nonvertebral** and **vertebral** fractures	hormone therapy can be used as **first-line therapy**
men requiring treatment of osteoporosis	prevention of fractures	- alendronate, risedronate and zoledronic acid can be used as **first-line therapies** - Testosterone is **not** recommended for the treatment of osteoporosis in men

- Alendronate is not without risk, we give it fo 5-10 years maximum. It works by preventing bone loss (inhibits osteoclasts)
- So we always question whether the patient needs alendronate now? Because we wanna utilize it as much as possible.
- So we assess if the patient will fracture easily. How? FRAX tool and get up & go test “examines how steady the patient’s gate is”

Medication	Side effects
High-dose calcium supplementation	increase the risk of renal calculi and cardiovascular events
Bisphosphonates	• self-limited flu-like symptoms "especially after the first dose of zoledronic acid by infusion" • osteonecrosis of the jaw "rare" risk is higher for those with: ➔ malignancy ➔ undergoing radiation and chemotherapy ➔ High-dose bisphosphonates for bone metastases or glucocorticoids ➔ Diabetes ➔ poor dental hygiene ➔ undergoing invasive ➔ dental procedures such as tooth extractions or implants • **Atypical fractures of the femur i**n the trochanteric neck, poor healing "rare" ➔ more common among those undergoing long-term bisphosphonate therapy ➔ Radiography or bone scanning (or both) should be considered for individuals who have been on long-term bisphosphonate therapy and who experience new thigh pain • esophageal cancer "controversial" • atrial fibrillation remains "controversial"
Denosumab	increase the risk of cellulitis
Raloxifene	increase the risk of thromboembolic events, including pulmonary embolism
hormone therapy	increase the risk of thromboembolic events, including pulmonary embolism
Teriparatide	• Hypercalciuria and hypercalcemia • both generally mild and resolve spontaneously or with discontinuation of calcium supplementation

Special groups:

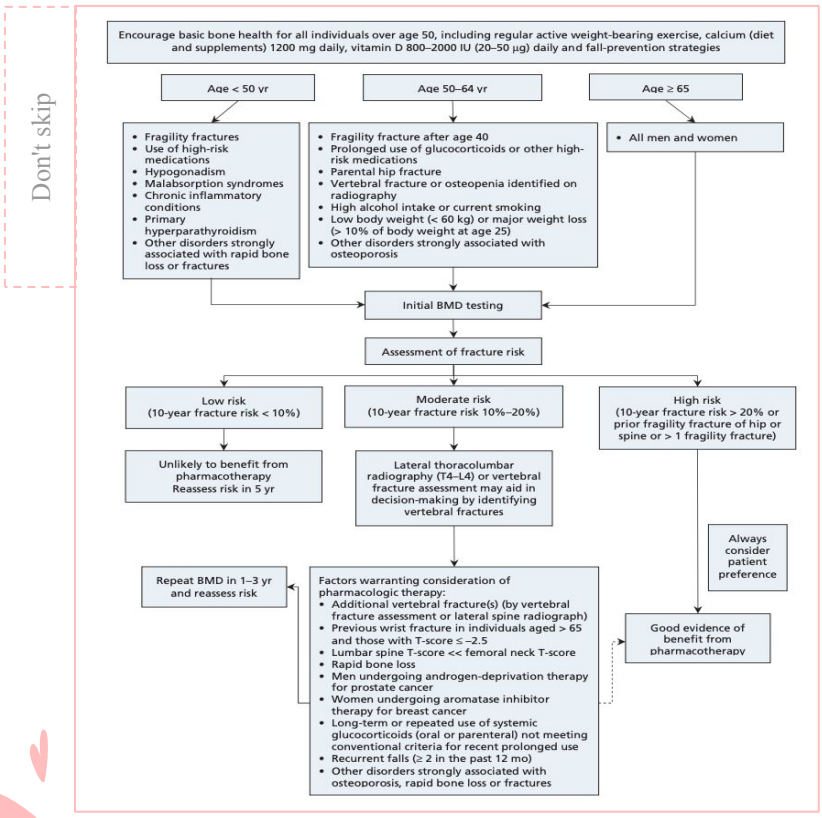
1. For individuals **over age 50** who are on **long-term glucocorticoid** therapy (≥ three months), a **bisphosphonate** (alendronate, risedronate, zoledronic acid) should be initiated at the outset and should be continued for at least the duration of the glucocorticoid therapy.
2. **Teriparatide** should be considered for those at high risk for fracture who are taking glucocorticoids (≥ three months).
3. For **long-term glucocorticoid** users who are **intolerant of first-line therapies**, calcitonin or etidronate may be considered for preventing loss of bone mineral density.
4. Women who are taking **aromatase inhibitors** and men who are undergoing **androgen-deprivation therapy** should be assessed for fracture risk, and osteoporosis therapy to prevent fractures.

How should I manage patients at risk of fracture?

- For all patients:
  - ➔ regular weight-bearing
  - ➔ balance and strengthening exercises
  - ➔ smoking cessation
  - ➔ optimization of total (dietary and supplements) calcium and vitamin D intake.
- For patients at risk of falls, fall-prevention strategies should be implemented.
- When choosing among therapies, the patient's individual risk profile, comorbid conditions, preferences and lifestyle should be considered.

Should I monitor therapy? If so, how often?

- For patients who are undergoing treatment, repeat measurement of bone mineral density should initially be performed after **one to three years.** "Testing interval can be increased once therapy is shown to be effective"
- **If bone mineral density has improved or remains unchanged, the patient is considered to have had a good response to therapy.**
- Continued loss of bone mineral density or a new fracture may reflect poor adherence with therapy, failure to respond to therapy or previously unrecognized secondary causes of osteoporosis.
- For moderate-risk individuals, including those with a T-score of –2.5 or below: repeat measurement of bone mineral density should be obtained after **one to three years** to monitor for rapid bone loss. If bone mineral density is stable, then less frequent monitoring can be considered.
- For individuals with low risk of fracture and without additional risk factors for rapid loss of bone mineral density, a testing interval of **5–10 years** may be sufficient.



When should I stop or use combination therapy?

- **vertebral fracture** decreased by 55% among those who continued alendronate therapy after five years of initial treatment (for a total of 10 years) relative to those who stopped after five years.
- Discontinuation of risedronate or hormone therapy (estrogen) may result in loss of bone mineral density.
- Combinations of hormone therapy or raloxifene with a bisphosphonate have yielded improvement in bone mineral density, however not in fracture reduction rate.
- Individuals at high risk for fracture should continue osteoporosis therapy **without** a drug holiday.
- Avoid simultaneously prescribing more than one antiresorptive agent for fracture reduction.
- We asses at 5 years.
- Decision factors whether to continue or give them a drug holiday are:
- 1) Response to bisphosphonates. 2) How high the risk of a fall is? If it is high, we won't stop it. If patient is active, responsive, lost weight then he is a candidate for a drug holiday.

When should I refer to a specialist?

- Fracture
- significant ongoing loss of bone mineral density despite good adherence while on first-line therapy
- Intolerance of first- and second-line therapies
- Secondary cause of osteoporosis that is outside the expertise of the primary care physician
- extremely low bone mineral density

Questions

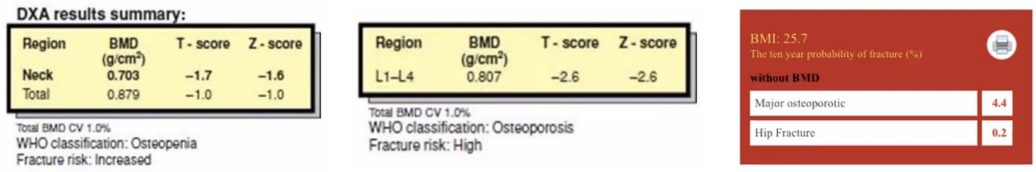
1. Samira is a 35 year old woman, came into your office because she will be getting married in 4 months and would like to start contraception. What will you offer? She is a smoker for 5 years (Shisha), she has no past medical conditions, her father is hypertensive, she swims twice per week, her BMI is 22, her BP in office is 102/70, she is anxious about getting pregnant in the first year of marriage.

A) Nothing, OCPs are contraindicated
B) Condoms, they are safe and reliable
C) Encourage pregnancy, she is getting old
D) Start OCP and offer information

2. You have decided to start Samira on OCP. What examination and tests do you want to do? You can do more than one.

A) Breast exam
B) Blood pressure
C) Pelvic exam
D) CBC
E) Liver function (ALT, AST, GGT, ALK)
F) Renal profile (Cr, electrolytes)
G) Lipid profile
H) Fasting blood sugar
I) Breast ultrasound
J) ECG

3. 52 Year old Sara comes in to review her DEXA scan. You calculate her FRAX score. What is your management? You can choose more than one.



A) Encourage her to increase activity
B) Advise her to increase calcium in diet
C) Prescribe calcium supplement
D) Advise her to spend more time in the sun
E) Prescribe Vitamin D supplement
F) Start alendronate
G) Start menopause hormone therapy
H) Order blood work

Answers:
1. D
2. B
3. A&B&C&D&E

Questions

4. All patients on bisphosphonates need to discontinue therapy after 5 years.

A) True
B) False

5. Layla came to your clinic crying “Doctor I can’t live like this!” assess her presentation and offer a suitable management. She is 55 years old presented with a hx of embarrassing hot flashes multiple times a day, difficulty sleeping as she sweats a lot requiring a change of clothes. LMP was 5 years ago, no past medical or surgical history, taking a multivitamin only. Not doing any exercise. Fhx: father HTN and MI, mother DM. O/E: BP 125/70, PR 62 regular. BMI 25. Non smoker.

A) There is nothing you can do, it is not a disease it is normal aging
B) Start SSRI or clonidine as they are first line therapy
C) Discourage her from HRT as it is very dangerous
D) Offer HRT to help relieve her symptoms

6. Menopause hormone therapy is not a safe option for patients

A) Yes! The risk of breast cancer is too high.
B) No! It depends on the patient’s own risks.

7. 25 year old Sahar presented to your clinic 4 days post NSVD wanting a prescription for formula, as she is not producing enough milk, how do you assess that?

8. Sahar starts crying and says “I’m not a good mom, I feel overwhelmed and sad.” What do you think of her symptoms?
She doesn’t sleep well because the baby wakes her up every few hours. She is forgetful during the day and finds it difficult to concentrate sometimes . Her appetite is up and down sometimes she eats a lot and sometimes she doesn’t feel like it. She is crying more than she ever did and feels scared by motherhood. She is at her mom’s house now and feels the family supports her. She has never had suicidal thoughts.

Answers:
4. B
5. D
6. B
7. Asses if the baby is gaining weight & urinating.
8. Postpartum blues

Questions

9. Fatima a 43 year old lady presents to your clinic for a check up?
Choose the age appropriate screening steps. You can choose more than one.

A) CBC, LFT, Renal Profile
B) Ask about past hx
C) Ask about family hx
D) Lipid profile panel
E) FBS, HgA1c
F) ECG
G) Blood pressure
H) Mammogram
I) DEXA
J) Colonoscopy or occult blood

10. During your history you discovered her mother and 2 maternal aunts have osteoporosis, will you offer her a DEXA?

A) No, it depends on the age her mother was diagnosed.
B) Yes of course! It is better to be safe than sorry
C) Not sure I might do blood tests for calcium and Vit D

Answers:
9. B&C&D&E&G&H
10. All answers are acceptable

Notes

1. She has risks but no absolute contraindication.

2. Not C because she isn't married. Not D because you shouldn't do labs without knowing what you're looking for. Labs don't diagnose, they either confirm or reject your ddx. Poke is harm and you could go down a rabbit hole. Blood pressure has to be done for documentation and medicolegal concerns. Others are done for specific concerns. We don't do coagulation profile for screening, it has false positive. G can be done (acceptable answer with B) because OCP's affect HDL & LDL levels, and we have familial hypercholesterolemia in our community.

3. She has osteopenia in femoral neck & osteoporosis in spine. However, it is reasonable not to start bisphosphonates, because according to the ten year probability of fracture, her risk of fracture is low. So we give her life style modification. This patient's spine is osteoporotic, if you enter her lumbar spine numbers instead of hip you'll find: major osteoporotic 6.6, hip fracture 09.
So, still low. We leave alendronate till we need it.

7. If the patient is gaining weight and urinating (6-10 wet diapers a day) then the patient is feeding. It's hard to go back to breastfeeding if the baby gets used to bottle feeding which is easy for him. You could weight the baby, ask mom to feed him then weight again, if increase it shows that the baby has fed.

8. Only difference from major depressive disorder is duration. Here only 4 days so postpartum blues. It's important to screen for suicidal and infanticidal thoughts in such case.

9. Ask about: anybody in the family has any cancer? Colon & ovarian cancers are high risk too, most common cause: sporadic gene mutation. Age is the highest risk factor. There is controversy about mammogram, family history is key here. DEXA is not necessary unless there is a strong family history. A is incorrect since anemia is usually detected earlier on during pregnancy or teenage years. We could do A too though since she is getting poked either way.

10. It depends on the age of diagnosis, if mother got it at 65 and your patient is 40 she's not a candidate for screening. But for example if her father, mother, aunts, maybe it's worthwhile to do it. D is done thinking about osteomalacia yet DEXA looks osteoporotic. You need to investigate it because it's reversible.