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MENOPAUSE NATIONAL GUIDELINES

FOR PRIMARY HEALTH CARE PROVIDERS IN IRAQ

DISCLAIMER
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1. Contents

Acronyms

PHC	Primary Health care
I-WISH	Iraqi Women socio and health indicators Survey
BMI	Body Mass Index
FDA	Food and Drug Administration
DEXA	dual energy X-ray absorptiometry
CHD	Coronary Heart Disease
LDL	Low Density Lipoprotien
HDL	High Density Lipoprotein
Lp	Lipid Profile
CVD	Cardiac Vascular Disease
HRT	Hormone Replacement Therapy
VT	Venous thrombosis
VTE	Venous Thrombosis Embolism
CA	Cancer
CU-IUD	Cupper- Intra Uterine Device
BMD	Bone Mineral Density

National guidelines for primary health care providers

Menopause

1. Purpose and scope

The aim of this guideline is to build the capacity of PHC physicians and providing them with up-to-date information about how to approach and counsel women at menopausal age in accordance with the local needs and requirements. It would be of help to set referral criteria for this particular woman health issues. It also raises the concept of menopause as a physiological phenomenon in Iraqi women, as there is lack of knowledge in that aspect and lack of specialized centers which provide services for such women at the level of primary health care centers or hospitals.

2. Definition

Menopause is defined as the time when there have been no menstrual periods for 12 consecutive months and there is no other biological or physiological cause identified. .[1] This is a natural event that normally occurs in women age 45 - 55. It is a retrospective diagnosis, where the woman has a permanent cessation of the primary functions of the ovaries. This transition is progressive occurring over a period of years, due to the fluctuation of hormonal levels produced by the aging ovaries. However, for some women, the accompanying signs and effects that can occur during the menopause transition years can significantly disrupt their daily activities and sense of well-being.

2.1 Changes in ovarian function

During the menopause transitional period, the age related number of ovarian follicles decrease and in response the follicle-stimulating hormone (FSH) increases. Levels of the gonadotropin hormone FSH will continue to be elevated in intent to stimulate the ovarian function but due to physiological changes in the ovary, this becomes increasingly resistant to stimulation by gonadotropins. It has been postulated that the FSH receptors become absent on the ovarian cells. As a consequence the ovarian hormones or estrogens such as Estradiol and Estrone are being produced in small amounts. Nevertheless, other parts of the ovarian tissue are still capable to produce other hormones such as androgens for a longer period of time even after the menopause had occurred. Once the menopause is established and the menstrual periods disappear, the woman is not able to conceive children any longer. [1, 2]

2.2 Basic menopausal definitions:

Menopause – Permanent cessation of menstruation. Retrospective diagnosis after 12 consecutive months of amenorrhoea.
Perimenopause – Starting from the first features of the approaching menopause (vasomotor symptoms, menstrual irregularity) and ending 12 months after the last menstrual period.
Postmenopause – Dating from the final menstrual period, but can only be defined after 12 months of spontaneous amenorrhoea.
Climacteric – Transition from reproductive to non-reproductive state. The menopause itself is a specific event during the climacteric.
Premature menopause – Menopause occurring before the age of 45 years.

2.3 Premature ovarian failure and early menopause

We consider a menopause premature when occurs in women younger of 40 years of age and an early menopause when it occurs before the age of 45 years. Premature menopause (premature ovarian failure) occurs in 0.9-1.2% of women; while early menopause affects approximately 5% -10% of women. Observational studies have identified a number of risk factors for early / premature menopause such as: smoking, ethnicity and positive family history. [3] It has been observed that genetic causes such as the Turner's syndrome and the fragile X chromosome syndrome can be associated with premature menopause. Premature menopause can also occur after the treatment of cancer such as leukemia's, lymphomas and gynecological cancers; in these cases we consider it as a side effect of the treatment or iatrogenic or secondary menopause. [4, 5]

We can consider that premature menopause is due to genetic or unknown causes (idiopathic) or could be secondary to treatments or other diseases. We present some of these causes in the table below: [6]

Primary	Secondary
Chromosome abnormalities	Chemotherapy and radiotherapy
Follicle-stimulating hormone receptor gene polymorphism and inhibin B mutation	Bilateral oophorectomy or surgical menopause
Enzyme deficiencies	Hysterectomy without oophorectomy/uterine embolization
Autoimmune diseases	Infection – HIV, mumps, TB
Idiopathic	

2.4 Epidemiology

Thanks to the advances of medicine, the life expectancy is improving. As a consequence more women will live many years (30-40% of her lifespan approximately) in a postmenopausal period with a decreased estrogen production [7, 8]

The average age of spontaneous natural menopause is 51 years (range 45-55 years). Observational studies indicate that African, African–American and Hispanic ethnicity and current smoking are factors associated with an earlier age of menopause. [3]

In Iraq, life expectancy for female reaches 61 years (*Reference: Iraqi Ministry of Planning/ Central Statistics Organization, 2011*). The Iraqi Women Integrated Social and Health survey (I-WISH) conducted in 2011, revealed that more than one million women over 55 years are living in Iraq (6.8% of the Iraqi female population), and 72.4% of those are expected to be illiterate. A baseline assessment in Iraq revealed that elderly women are going through tremendous pressure as they are expected to take care of other family members with special needs such as disabled or sick while they themselves due to age and disease need health and social assistance. 35% of those women reported that their health status is poor or very poor and 31.1% need assistance for feeding, getting dressed, using the bathroom and for moving around, 11% reported feeling unhappy with their life in general (6.4% in Kurdistan and 11.4% in other areas). Another study conducted by the Nursing College, Baghdad University, in the year 2000 including 410 women aged between 40-60 years, investigating the factors affecting the age of natural menopause, concluded that the mean age for menopause was 49.4 $\pm$ 3.2 years and the significant predictors for that age were; gradual menstrual cessation, hormonal contraception use for long duration and negative history of abortion.

3. Approach to menopausal women

3.1 Symptoms of menopause

The fall in oestrogen levels that occurs at the menopause can cause a variety of symptoms. Although the list seems alarming, few women experience all of these symptoms and some

women are fortunate enough to have no obvious problems. From a medical perspective, the immediate symptoms are mostly harmless, and it is the longer-term consequences of oestrogen deficiency on the skeletal system that cause greater concern.

Changes in menstrual pattern:
As ovulatory cycles begin to predominate, the length of the menstrual cycle begins to vary and gaps of several weeks or months may occur between menstrual periods. Most women find their periods become lighter during the peri-menopause, but some experience more frequent and heavier bleeding before their periods eventually stop. Because of the possibility of renewed follicular activity, women can become pregnant even at this stage of life. They should be advised to continue with contraception for two years after their last period if it occurred before the age of 50 and for one year if it occurred after the age of 50.

3.2 Immediate effects of oestrogen deficienc

Vasomotor:

It is estimated that about 70% of women experience vasomotor symptoms. These symptoms are:

- Hot flushes
- Night sweats
- Palpitations
- Headaches

Vasomotor symptoms are commonly more intense in the previous two or three years before the periods end, but they may continue for many years afterwards.

A study conducted in Baghdad city, looking for the prevalence of vasomotor symptoms found that the prevalence of hot flushes among pre-menopausal women is (21.9%) and this proportion rises to (64.9%) and (87.6%) respectively among pre-menopause and post-menopause women. The study attributed such high prevalence of vasomotor symptoms in comparison with women from other countries to the prior poor health status, premenstrual and menstrual symptoms (e.g. dysmenorrhea,…etc), low socioeconomic level, unavailability of hormonal replacement therapy, and that uninformed or misinformed women regarding menopause may have its impact on women's perception of climacteric complains. (*Reference: Abdul Amir F. Assessment of the natural climacteric complaints among middle age Iraqi women in Baghdad city. Al-Taqani J 2006; 19(1): 106-16.*).

3.3 Medium-term effects of oestrogen deficiency

Urogenital symptoms:
The vagina and distal urethra are estrogen dependent tissues. The falling estrogen levels in post-menopausal women lead to a marked drop in vaginal and vulvar capillary blood supply causing

the skin to appear red and dry. Additionally there is a loss of collagen from the underlying tissues. These two factors cause the vaginal epithelium to become thinner and less elastic and the vagina narrower and shorter causing anthropic vaginitis. As secretions lessen, there is a higher risk of vaginal infections. At least 50% of women will suffer from one of the following symptoms:

* Vaginal problems - Dyspareunia
  - Vaginitis

* Urinary problems: - Frequency
  - Urgency

Generalized Connective tissue atrophy

Oestrogen helps maintain the epidermis, so changes in the skin, nails and hair are common when oestrogen levels fall. Women may find their skin becomes dry, inelastic and is easily broken or bruised. The loss of thickness and elasticity is largely due to a decline in collagen levels. Other symptoms of connective tissue atrophy are brittle nails, hair loss, muscular aches, bone and joint pain. These changes in the connective tissue canal promote vaginal prolapse and the subsequent development of stress incontinence-dysuria and these represent an additional effect of Oestrogen deficiency on the urogenital system after menopause.

3.4Late effect of estrogen deficiency (osteoporosis, cardiovascular, cancers)

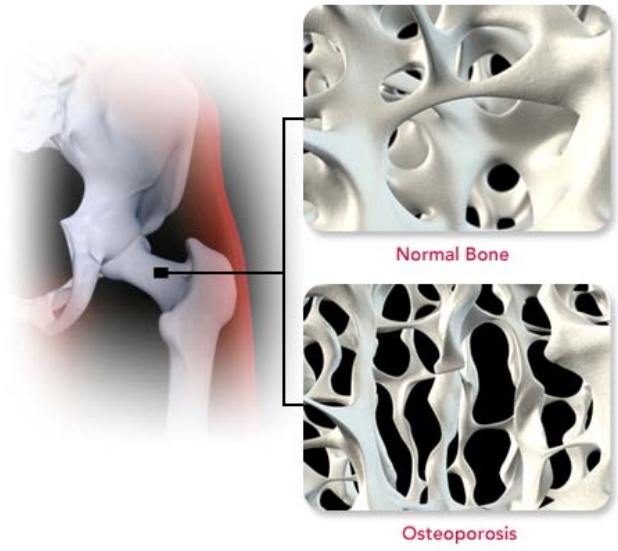
4.1 Osteopenia/Osteoporosis

Osteopenia means that your bone mineral density is somewhat lower than "normal" but not low enough to be osteoporosis. Bone mineral density is a measurement of the level of minerals in the bones, which shows how dense they are. Bone mineral density is found using a bone density test. Osteopenia is defined as a bone mineral density T-score between -1.0 and -2.5.

It is important to note that having osteopenia is not the same as having osteoporosis, and that technically, osteopenia is not in and of itself a disease, as osteoporosis is. Instead, osteopenia is an indication that your BMD is below the statistical norm and that you could eventually develop osteoporosis or be at risk of a future fracture.

Osteoporosis is a skeletal disease marked by low bone mass and micro architectural deterioration that leads to an increased susceptibility to fracture .

It is preventable and treatable disease, but due to the absence of warning signs prior to a fracture, many people is not diagnosed in time to receive effective therapy during the early phase of the disease .



The most common fractures are those of the vertebrae (spine), proximal femur (hip) and distal forearm (wrist).The process of bone remodeling that maintains a healthy skeleton may be considered a preventive maintenance program (continually removing older bone and replacing it with new bone). Bone loss occurs when this balance is altered, resulting in greater bone removal than replacement. The imbalance occurs with menopause and advancing age. With the onset of menopause, the rate of bone remodeling increases, magnifying the impact of the remodeling imbalance. The loss of bone tissue leads to disordered skeletal architecture and an increase in fracture risk.

Diagnosis of Osteoporosis and Fracture

Diagnosis is based on bone mineral density (BMD) measurement. Dual-Energy X-Ray Absorptiometry (DEXA) is the central device most commonly used and is currently the gold standard for both patient care and clinical investigation in osteoporosis.

Listed below are several osteoporosis risk factors:

- Getting older, which increases your risk of osteoporosis because bones become weaker as you age?
- Ethnicity — for instance, women who are white or of Southeast Asian descent have the greatest risk of osteoporosis, and African-American and Hispanic men and women have a lower, but still significant, risk of the disease
- Low body weight, or under 125 pounds (56.7 kilograms) if you're of average height
- A personal history of fractures after age 40
- A parental history of osteoporosis or hip fractures

- Using certain medications that can cause bone loss, especially steroids
- Eating disorders or metabolism problems that do not allow the body to take in and use enough vitamins and minerals
- Chemotherapy, or medicines such as steroids used to treat a number of conditions, including asthma
- Exposure to radiation

  In addition, having a family history of osteoporosis, getting limited physical activity, smoking, regularly drinking soda, and drinking excessive amounts of alcohol also increase the risk of osteopenia and, eventually, osteoporosis.

Management of Osteopenia/Osteoporosis

Osteopenia is treated by taking steps to keep it from progressing to osteoporosis

1. **Non Pharmacologic Therapy:**

Lifestyle modification includes:

- Adequate intake of calcium and vitamin D. The recommended intake of calcium is 1200 mg/day from dietary intake and supplement, and for Vitamin D are 400- 800 IU/ day in addition to sun exposure for 10-15 minutes of the face, hands arms 2-3 times a week.
- An active lifestyle including regular weight-bearing and muscle-strengthening exercise to reduce the risk of falls and fractures.
- Avoidance of cigarette smoking, high intake of caffeine or alcohol.

Your body doesn't produce calcium on its own, so you must obtain it through other sources. Calcium can be found in a variety of foods, including:

- Dairy products, such as cheese, milk and yogurt
- Dark green leafy vegetables, such as broccoli and kale
- Fish with soft bones that you can eat, such as sardines and canned salmon
- Calcium-fortified foods and beverages, such as soy products, cereal and fruit juices

2. **Pharmacologic Therapy:**

A number of pharmacological agents are approved by FDA for the treatment of osteoporosis. All increase bone mineral density and reduce the risk of fractures:

2.1. Bisphosphonates:

They have been shown to slow bone loss, increase bone density, and reduce the risk of spine and non-spine fractures. They may be considered in postmenopausal women who are at risk of

developing osteoporosis and for whom the desired clinical outcome is to maintain bone mass and to reduce the risk of fracture

- **Alendronate** (Fosamax or Fosamax Plus D) (10 mg daily tablet, 70 mg weekly tablet or liquid formulation, and 70 mg weekly tablet with 2,800 IU or 5,600 IU of vitamin D3) to increase bone mass. It is proved to reduce fracture by 50%over three years of treatment.
- **Risedronate sodium**.: Actonel® or Actonel® with Calcium , Atelvia)
  (5 mg daily tablet; 35 mg weekly tablet; 35 mg weekly tablet packaged with 6 tablets of 500 mg calcium carbonate; 75 mg tablets on two consecutive days every month; and 150 mg monthly tablet). It increases bone mass and reduces the incidence of vertebral fractures.

Bisphosphonates need to be taken on an empty stomach early in the morning with no food for at least 30 minutes afterwards. Main side effects include stomach upset and heartburn, if severe, IV formulations can be used. Treatment is usually maintained for 5 years.

2.2. Calcitonin: (Miacalcin or Fortical)

It is delivered as a single daily intranasal spray that provides 200 IU of the drug. Subcutaneous administration by injection also is available. It is used for women who are at least five years postmenopausal.

2.3. Estrogen/Hormone Therapy (ET/HT)

Estrogen Therapy (ET) and Hormone Therapy (HT) include:

- ET : Climara, Estrace, Estraderm, Estratab, Ogen, Ortho-Est, Premarin, Vivelle.
- HT: Activella, Femhrt, Premphase, Prempro.

It is effective for the prevention of osteoporosis, relief of vasomotor symptoms and vulvo-vaginal atrophy associated with menopause. Nevertheless, the risk associated with the ET outweighs the benefits in women older than 60 years and shouldn't be used.

HT prescription will differ depending on:

- If the woman has uterus, she can be prescribed a combination of estrogen plus progestin.
- If the woman doesn't have a uterus, then only one hormone, estrogen (ET) is prescribed.

The administration of the HT could be done by:

- a pill taken by mouth
- a patch, cream, gel, or spray that can be applied to the skin
- a cream, suppository or ring that can be used with in the vagina

The Woman's Health Initiative (WHI) found that five years of HT (Prempro®) reduced the risk of clinical vertebral fractures and hip fractures by 34 percent. Because of the risks of cardiovascular diseases and breast cancer, ET/HT should be used in the lowest effective doses for the shortest duration to meet treatment goals. It is no longer regarded as a front line option for the prevention or the treatment of osteoporosis in postmenopausal women. Their use is limited to:

1. Women who have both osteoporosis and menopausal symptoms which is severe enough to affect life quality.

2. Premature menopause (at age <40) until they are 50 years old, if this is not associated with any increasing health risk.

2.4. Other therapeutic options to treat osteoporosis:

- **Estrogen Agonist/Antagonist (formerly known as SERMs-Selective estrogen receptor modulators) :**
  There are three SERMs:

  tamoxifen (also called tamoxifen citrate; brand name: Nolvadex)
  Evista (chemical name: raloxifene)
  Fareston (chemical name: toremifene)
  Each is a pill, usually taken once a day. Tamoxifen is the oldest, most well-known, and most-prescribed SERM.
  SERMs can be used to treat women both before and after menopause.
  Raloxifen (Evista):
  Is indicated for reducing the risk of invasive breast cancer in postmenopausal women with osteoporosis. It does not reduce the risk of coronary heart disease. Similar to estrogen, Raloxifene may increase the risk of deep vein thrombosis. It also increases hot flashes and make it worse (which is the main symptom of menopause worsen). It reduces the risk of spinal fracture but not those of the hip or the wrist.

- **Parathyroid hormone**

  Teriparatide: PTH (1-34) (Forteo) is anabolic agent administered by daily subcutaneous injection. It is recommended for treatment of osteoporosis associated with glucocorticoid therapy. Because it has been associated with osteosarcoma in animal experimental studies, patients with increased risk of bone malignancy should not use it.

- **Combination therapy**

Combination therapy with bishphosponate and non bisphosponate can provide additional increase in BMD as compared to monotherapy. However, the cost and potential side effects should be weighed against potential gains.

Prevention of Osteoporosis and/or Fracture

Health workers should provide the following services to menopausal women:

- Counsel on the risk of osteoporosis and related fractures.
- Check for secondary causes.
- Advise intake of adequate amounts of calcium and vitamin D including supplements if necessary.
- Recommend regular weight-bearing and muscle-strengthening exercise to reduce the risk of falls and fractures.
- Advise avoidance of tobacco smoking and excessive caffeine and alcohol intake.
- Recommend BMD testing as indicated.
- Initiate prophylactic treatment as indicated.

3.4.2 Cardiovascular diseases (CVD)

After menopause, women are more likely to have heart disease and stroke. By the time a woman reaches the age of 60, the gap in incidence of coronary heart disease (CHD) between men and women is greatly reduced. Cardiovascular disease is the leading cause of death and an important contributor to morbidity and disability in women. Stroke, in particular, is especially prevalent in older postmenopausal woman.

The risk is thought to be due to the withdrawal of the protective effect of oestrogen around the time of the menopause.

The effect of hormones on cardiovascular function may be attributed to the changes encountered on lipids, homeostasis, and carbohydrate metabolism, in addition to other direct effects of estrogen including modulation of blood vessel reactivity in the short term and vascular structural remodeling in the long term.

However, it might also be due to the fact that around menopause, a clustering of obesity, hypertension and dyslipidemia is often seen. Similarly polycystic ovary syndrome is also linked with cardiovascular risk factors and more adverse CHD events post-menopause.
Premature loss of ovarian function and estrogen deficiency is associated with increased risk of calcified plaque in coronary arteries.

Hormone replacement therapy and cardiovascular Diseases:

Physicians who are responsible for the care of women must consider the potential benefit and risk of therapy for both treating symptoms and potentially preventing disease with hormone replacement therapy (HRT), which has complex cardiovascular effects that are modulated by the type of HRT and a woman's own cardiovascular risk.

Estrogen has both rapid and longer-term actions on the cardiovascular system. These rapid actions are non-genomic and cause vasodilatation. The longer-term actions are genomic, mediated by estrogen receptors, and affect vascular injury responses and atherosclerosis. Thus estrogen may promote cardio-protective effects by reducing LDL cholesterol, raising HDL cholesterol, inhibiting oxidation of LDL particles, improving endothelial function and lowering levels of factors such as Lp(a), fibrinogen, and plasminogen activator inhibitor type 1.

On the other hand, adverse physiological effects on inflammation (as measured by C-reactive protein) and markers of thrombosis may counteract the beneficial effects and may also be important in the observed increased risk of stroke and venous thromboembolism.

In contrast to oral hormone therapy, transdermal estrogen does not have significant effects on some markers of thrombosis or inflammation. The addition of progestins modulates estrogen's cardiovascular effects; however, non-androgenic progestins may have fewer adverse effects.
Observational studies of primary prevention of CVD have consistently shown that postmenopausal women who use estrogen with or without a progestin have a lower rate of coronary events than those who do not. However, meta-analysis of these observational studies did not show any evidence of overall protection from CVD once results were controlled for confounding factors such as socioeconomic status, education, and major coronary risk factors.

Clinical trials in women with established coronary artery disease concluded that HRT does not prevent secondary attacks. It may even increase the risk of progression of atherosclerosis in the first year of treatment in older postmenopausal women.

HRT and stroke

Observational studies as well as clinical trials reported that HRT (predominantly with estrogen) increases the risk of stroke, especially in older postmenopausal woman with risk factors for these conditions. They indicated that postmenopausal HRT is not effective for reducing the risk of a recurrent stroke among women with established vascular disease or for preventing a first stroke.

Venous thrombosis (VT)

Observational studies have shown increased risk for deep venous thrombosis and pulmonary embolism in postmenopausal women prescribed HRT with the an additive risk with known risk factors of thrombosis such as increasing age, overweight, and obesity, as well as Factor V Leiden. It is also indicated that the risk is higher among postmenopausal women with known cardiovascular diseases.

Management of Cardiovascular diseases:

There are persisting data showing that Cardiovascular Disease is undertreated in women or that women do not recognize the importance of CVD. Efforts should focus on reducing the risk of CVD among women in effective ways.

Cardiovascular risk factors in particular should be addressed and treated as per guidelines. Women should receive counseling about lifestyle modifications (smoking cessation, maintenance of a normal body weight, regular moderate to vigorous physical activity, and consumption of a heart-healthy diet). In addition, pharmacotherapy of hypertension and dyslipidemias should be used when indicated for women who already have established heart disease or who have been identified as high risk according to risk calculations.

Control of hypertension and diabetes assume heightened importance because of their greater mortality associated with acute coronary events, such as myocardial infarction and worse outcomes from stroke.

Therapy with anti-platelet agents (such as acetylsalicylic acid), beta blockers, angiotensin-converting enzyme inhibitors, and lipid-lowering medications is recommended when indicated and is amply supported by evidence of benefit.

Women on HRT who experience a cardiovascular event such as myocardial infarction, stroke, or venous thromboembolism should be advised to discontinue such therapy. Should significant vasomotor symptoms require continuation of HRT, then the lowest dose for the shortest time should be considered.

In light of available alternative for enhancing cardiac health in menopausal women, HRT should not be used for primary or secondary prevention and the role of HRT in the prevention of such disorders remains controversial.

Available evidences for the use of HRT in such cases are as follow:

1. Health care providers should not initiate or continue HRT for the sole purpose of preventing CVD (CAD and stroke).
2. Health care providers should abstain from prescribing HRT in women at high risk for venous thrombosis embolism (VTE).
3. Health care providers should consider other evidence based therapies and interventions to effectively reduce the risk of CVD events in women with or without vascular disease.

3.4 Psychological and social issues associated with menopause

Psychosocial influences have been found to impact on the symptoms a woman may experience as she moves through the menopause transition. Consequently any assessment of the menopausal woman should include an exploration and understanding of how psychosocial factors influence the experience of menopause and midlife. For some women, the accompanying signs and effects that can occur during the menopause transition years can significantly disrupt their daily activities and sense of wellbeing. In addition, women who have some sort of functional disorder

affecting the reproductive system (e.g., endometriosis, polycystic ovary syndrome, cancer of the reproductive organs) can go into menopause at a younger age than the normal timeframe. These functional disorders create more significant health problems, both physical and emotional, for the affected woman.

It is unclear why psychological symptoms occur at the menopause, and they may well have little to do with hormonal fluctuations. Life stresses at this age are an obvious causative factor. Many women do not realize that the following symptoms are very normal at this stage of life and fear they may be on the verge of a break down. Symptoms may include[1]: Mood swings, irritability, depressed mood, insomnia or other sleep problems, forgetfulness and difficulty in concentrating, and decline in sexual desire

Society and culture:

The cultural context within which a woman lives can have a significant impact on the way she experiences the menopausal transition. Research indicates that whether a woman views menopause as a medical issue or an expected life change is correlated with her socio-economic status.

Sexual function
Sexual problems are common complaint during the climacteric time and post-menopause, about a third of women will complain of a loss of libido. However there is a complex relation between sexuality and the menopause.

3.5 Clinical examination of menopausal women

Examination of menopausal women should include:

General physical examination:

- Including anthropometrics measures, body mass index (BMI) and vital signs mainly Blood pressure (BP).
- Breast examination.
- Pelvic examination.

A holistic approach to health status should be taken, rather than simply looking for features of menopause in isolation. A thorough assessment of the cardiovascular system, respiratory system and musculoskeletal system may detect common age-related health problems, and help to create a management plan. In addition, clinical examination also looks for physical features of menopause such as dry hair and skin, and evaluation of thyroid status, Specific system examination, depending on the symptom presentation.

[1]Dealing with the symptoms of menopause.
http://www.health.harvard.edu/newsweek/Dealing_with_the_symptoms_of_menopause.htm

Breast examination needs to be carried out regularly due to an increased risk of breast cancer as women get older. (Annex: Risk Factor for breast cancer)

Pelvic examination is carried out to assess for the presences of complications of menopause such as urogenital atrophy. A bimanual examination should be performed to exclude pelvic pathology such as ovarian cysts or fibroids, especially following hysterectomy where the ovaries have been conserved. Gynecological examination, including a Pap smear according to national guideline for testing or, if there is abnormal vaginal bleeding or a previous abnormal smear.

3.6 Investigations needed for menopausal women

Confirmation of menopause
The diagnosis of the menopause can usually be ascertained from a characteristic history of the vasomotor symptoms of hot flushes and night sweats and prolonged episodes of amenorrhea. Measurement of plasma hormone levels in patients with classical symptoms are unnecessary, expensive, time consuming and of little clinical significance. So history is considered more relevant than hormone levels, as a wide variation of levels around the menopause.

Follicle-stimulating hormone (FSH):
FSH estimation is helpful in cases of premature menopause. Two levels of FSH > 30 IU six weeks apart is consistent with ovarian failure.

Laboratory assessment tests:

1. **Lipid profile & fasting glucose:** may be useful in women with risk factors not only from a general screening point, but also if the patient is contemplating starting HRT. If abnormal lipids are detected, it should be corrected by diet and statins, if appropriate on an individual basis, before HRT is commenced.

2. **Thyroid Stimulating Hormone (TSH) levels:** indicated where there are symptoms of thyroid dysfunction or palpable thyroid, which may manifest around the time of the menopause.

3. **Coagulation studies:** Where past history of thrombo-embolism (particularly if spontaneous) or pulmonary embolism, and/or if less than 40 years old (Where family history or known familial disorder could be detected).

4. **Full blood examination, iron studies:** When abnormal bleeding, especially menorrhagia exists.

5. **Urodynamic Assessment:** Where there is a history of stress and/or urge incontinence, to determine the severity of the incontinence. The result will aid in planning and managing the symptoms.

6. **Vaginal ultrasound:**

- To assess endometrial thickness where there is abnormal vaginal bleeding, >4mm thickness in the post-menopausal woman requires endometrial sampling either by endometrial biopsy or hysteroscopy and curettage.
- To exclude endometrial pathology such as polyps or submucous fibroids.
- To exclude pelvic pathology such as ovarian cysts or fibroids.

Consider the following:

- Referral to a gynecologist is appropriate for further investigations such as hysteroscopy and endometrial biopsy/D&C, where the ultrasound shows an increased endometrial thickening greater than 4mm in the post menopause, pelvic pathology or with any postmenopausal bleeding.

- Endometrial biopsy is not a necessary prerequisite to treatment with HRT unless there are symptoms of postmenopausal bleeding or irregular perimenopausal bleeding.

7. **Mammogram with/without breast ultrasound:** If any breast abnormality is found on examination.

8. **Bone assessment:** Bone density: There are different techniques for establishing bone density. The most reproducible form is the DEXA (dual energy X-ray absorptiometry), which scans both the lumbar spine and the femoral neck. The Royal College of Physicians has issued guidelines as to which high-risk patients should be targeted for DEXA screening and that DEXAs are performed no more frequently for screening than every 2 years.

9. **Pap smear:**

The pap smear indications for women at any age in Iraq should be consistent with the National Program for cervical screening approved in Iraq in 2010 by MOH .
The National screening program recommends that:

- All women should have three times smear per life time with a 10-year interval between each smear commencing at an age not less than 25 years (25-45 years) or at least one smear for all women who had previous sexual contact and they are between of 35-45 years old .
- A woman should be screened if she had previous abnormal smear (dysplasia or HPV changes) within the last two years.
- A smear every two years following hysterectomy for women who ever had an abnormal pap smear or cancer of the cervix or uterus.
- A smear should be performed for any woman presenting with abnormal vaginal bleeding.

10. **Mammogram with/ without breast ultrasound**

- Mammography should be performed as part of the national screening programme for breast cancer yearly for women with risk factor for CA breast and every 3 years for women above 50 years if they do not have any risk factor unless more frequent examinations are clinically indicated. (See Annex for risk factors).
- In women over 45 years of age it is best to arrange screening before starting estrogen therapy to identify patients with sub-clinical disease.

11. Cardiovascular screening

Menopause brings changes in the level of fats in a woman's blood. These fats, LDL cholesterol appears to increase while HDL decreases in postmenopausal women as a direct result of estrogen deficiency.

Elevated LDL and total cholesterol levels peak in women at 55-65; about 10 years later than the peak in men which can lead to stroke, heart attack, and death.

4. Care plan for menopausal women

4.1 Health education

Many women arrive at their menopause transition years without knowing anything about what they might expect, or when or how the process might happen, and how long it might take. As a result, a woman who happens to undergo a strong perimenopause may become confused and anxious, fearing that something abnormal is happening to her. Hence, there is a strong need for information and more education on this subject.

4.2 Psychological support

The increased depression rate encountered during menopause suggests that it is not actually the hormonal changes, but the psychological impact associated with this stage that causes the problems.

While everyone agrees that dealing with all the physical changes that occur during menopause is not easy, most psychologists feel that depression during this stage is more a matter of attitude. The changes associated with menopause can be viewed from a different angle. During this stage, women can explore their creativity and social potential and expand their contribution to society. Women that have a positive attitude on the changes that happen in their body look healthier. Other studies have proved that negative attitudes on menopause also increase the unpleasant symptoms associated with it, such as hot flashes, fatigue, night sweats, sleeping disorders and aches.

4.3 Counseling

Individual counseling can be helpful to handle sad, depressed, anxious or confused feelings women may be having as they pass through this challenging transition time.

Counseling Women about Menopause: Consider the following:

- Face-to-face contact between a patient and clinician is most effective. However, there are many methods of providing information to patients, such as educational sessions, printed materials, audio and videotape.
- The objectives of counseling include addressing women's questions and concerns and enhancing the patient's confidence in the decision made to modify her life style. A partnership between clinician and patient characterized by mutual respect and trust enhances counseling.
- If Drug therapy is chosen, the patient and clinician should agree on the goals, whether they are short term (menopause symptom relief), long-term (primary or secondary prevention of diseases associated with aging), or both.
- The woman may experience troublesome side effects from pharmacologic agents, or fail to experience the expected or desired results. If the treatment decision was one made in partnership with her clinician, a woman is more likely to consult with the clinician before changing or discontinuing her treatment plan.

The messages that are recommended to communicate to women going through menopause:

Keep cool

Hot flushes and night sweats are the most common symptoms of the menopause. They're caused by a malfunction in the body's normal methods of temperature control. They can occur even before the periods have stopped but are most common in the first year after the last period.

To ease hot flushes and night sweats:

- Wear lighter clothing.
- Keep your bedroom cool at night.
- Try to reduce your stress levels.
- Avoid potential triggers, such as spicy food, caffeine, smoking and alcohol.

Try to relax

Psychological symptoms can include feeling down, anxiety, irritability, mood swings, tiredness and lack of energy. Because of the stress associated with menopause, it can be difficult to confirm if the psychological symptoms are a direct result of the menopause.

The following tactics can help improve the menopausal woman's mood:

- Getting plenty of rest.
- Regular exercise.
- Relaxation exercises such as yoga.

Sleep well

Restful sleep will help you cope with night sweats and other menopausal symptoms. Improve your sleep by:

- Avoiding exercise within two hours of bedtime.
- Going to bed at the same time every night.

Get some exercise

There's evidence that women who are more active tend to suffer less from the symptoms of the menopause. Exercise is important not only for the relief of short-term symptoms but also to protect the body from heart disease and osteoporosis. The benefits of exercise in preventing bone loss and fractures are well known. Brisk walking about three times a week is a cheap, easy and great way to start exercising.

Stop smoking

Women who smoke have an earlier menopause than non-smokers, have worse flushes and often don't respond as well to tablet forms of HRT. It is never too late to stop smoking.

Designing an Approach for Menopause Counseling

- Make an effort to address all of the Women's questions, Treat the woman's questions respectfully, even if her facts or sources are not ones you endorse.
- Educate the woman about relevant health conditions (such as heart disease and osteoporosis) so she appreciates how these diseases could affect her quality of life in the future.
- Discuss the known risks and benefits associated with each management option, and present in lay terminology information about the strength of the existing evidence and what remains unknown.
- Personalize the discussions based on the woman's need, health, social history, and family history.
- Consider the patient's preferences, values, and key concerns (e.g., family members' experiences, concern about breast cancer, etc.).
- Tailor the use of educational materials to the needs and wants of the woman and that briefly summarize relevant information.
- Consider with the woman practical issues that she may face if medication will be part of her management plan, such as cost, convenience, and side effects that might affect her desire to continue therapy.
- Ensure that follow-up is routinely done with all women who start a treatment with HRT regimen or any other pharmacological therapy. The interval for follow-up depends on the patient's needs and concerns.

4.4 Treatment

4.4.1 Life style measures

Diet

Some risk factors associated with aging and menopause cannot be changed. However, healthy eating and regular physical exercise can prevent or reduce certain conditions that may develop during and after menopause. The following dietary advice is recommended:

- Getting enough calcium: Eating and drinking 2 to 4 servings of dairy products and calcium-rich foods. Calcium is found in dairy products and fish.
- Increase iron intake: Eating at least 3 servings of iron-rich foods a day. Iron is found in lean red meat, poultry, fish, eggs, leafy green vegetables, nuts and enriched grain products.
- Getting enough fiber: Food high in fiber include whole-grain breads, cereals, pasta, rice, fresh fruits and vegetables.
- Eating fruits and vegetables: Include at least 2 to 4 servings of fruits and 3 to 5 servings of vegetables daily.
- Drink plenty of water: Drink at least eight 8-ounce glasses of water a day.
- Maintain a healthy weight: Lose weight (if overweight) by cutting down on portion sizes and reducing foods high in fat, not by skipping meals.
- Reduce foods high in fat: Fat should provide 30 percent or less of the total daily calories. Also, limit saturated fat to less than 10 percent of the total daily calories. Saturated fat raises cholesterol and increases the risk of heart disease. Saturated fat is found in fatty meats, whole milk, ice cream and cheese. Limit cholesterol intake to 300 milligrams (mg) or less per day.
- Use sugar and salt in moderation: Too much sodium in the diet is linked to high blood pressure. Also, reduce smoked, salt-cured and charbroiled foods – these foods contain high levels of nitrates, which have been linked to cancer.
- Avoid smoking.
- Exercise: Exercise is the most beneficial activity for women in their menopausal years. Postmenopausal women who exercise regularly are about half as likely to develop diabetes as their more sedentary counterparts. Women who exercised more than four times per week had half the risk of diabetes compared with women who never or rarely exercised (moderately or vigorously).

4.4.2 Hormone replacement therapy

As mentioned before under Cardiovascular Diseases (CVD), HRT is one of the options for the treatment of Osteoporosis. Choosing whether or not to use postmenopausal hormone therapy is an important health decision. There are two main types of hormone replacement therapy:

- **Estrogen Therapy:** Estrogen is taken alone.

- **Progesterone/Progestin-Estrogen Hormone Therapy:** Also called combination therapy, this form of HRT combines doses of estrogen and progesterone (progestin is a synthetic form of progesterone).

Types of Preparations available globally:

Preparations for estrogen therapy and combination therapy include oral, transdermal, injectable, and vaginal formulations. Transdermal delivery systems include patches, gels, sprays, and lotions, while vaginal products include suppositories, creams, and rings. Because of the potential risks and existing controversies regarding high-dose oral regimens, the popularity of low-dose preparations and different delivery systems (e.g., transdermal patches, gels, and lotions) is increasing. One vaginal preparation, the estradiol acetate ring, delivers a systemic dose of estradiol is available. Non oral preparations avoid a first-pass hepatic effect. Therefore, they may not produce changes in lipids, clotting factors, and inflammatory markers. As a result, they may possibly decrease health risks and adverse effects. Data have indicated that transdermal preparations, when compared with oral estrogen, are not associated with an increased risk of venous thromboembolism.

Estrogen:

Minimum effective dose of oestradiol should be used and increase accordingly,(there is a dose-response effects with venous thromboembolism and stroke). With lower dose of estrogen, there is less likely for woman to have breast tenderness, endometrial stimulation and associated bleeding problem.
The goal of treatment is to get the most physiological state possible with 2:1 oestradiol: oestrone ratio. It is better to avoid the oral rout, since the oral preparation are partially metabolized in the liver by hepatic first-pass metabolism and the thromboembolic risk is also neutralized by avoidance of first pass stimulation of coagulation factors, even in woman who are obese and thrombophilic.

Doses: twice weekly or once weekly transdermal systems containing both estrogen and progetogen as combined HRT. Oestradiol is also available as low volume daily trandermal gel.

Local (vaginal) eostrogen, as cream, tablets and ring containing oestriol and oestardiol will not cause endometrial hyperplasia according and can be used safely without adding progestogens. Oestradiol vaginal tab (25ug) is effective in relieving menopausal symptoms and urogenital symptoms without causing endometrial hyperplasia. The conjugated equine oestrogen cream will cause endometrial hyperplasia and should include a progestogen added to the formulation to prevent this adverse effect.

Recommended starting dose of currently available systemic estrogen:
- 0.3 mg oral conjugated equine estrogens.
- 1 mg oral micronized oestradiol or oestradiol valerate.
- 25-50 mcg transdermal oestardiol.
- Two (0.5) metered doses of oestradiol gel.
- 25-50 mg of implanted oestardiol.

Note: Larger dose may be needed in those with premature ovarian failure

- There are twice weekly or once weekly transdermal systems containing both estrogen and progetogen as combined HRT. Oestradiol also available as low volume daily trandermal gel.
- Local (vaginal) eostrogen, as cream, tablets and ring containing oestriol and oestardiol. They are not producing endometrial hyperplasia according to the available evidence and can be used without progestogenic opposition in low dose preparation. 25ug oestradiol vaginal tab. is effective in relieving menopausal symptoms, and a continuous year of use is very effective in relieving urogenital symptoms with no endometrial effects. The conjugated equine oesrtogen cream that causes endometrial hyperplasia requires progestogenic opposition after 3 months.

estrogens / progestagens:

A combination therapy with estrogens and progestagens regimen should be used (continuous estrogen + progesterone for 12-14 days / month) when the HRT is initiated within the first year after the last menstrual period occurred. If the woman had a previous subtotal hysterectomy done, progesterone should be given after 3-6 months of estrogen therapy initiation in case of any residual endometrium left.

Minimum dose of progesterone given orally in HRT in the sequential combined daily dose (in continuous dose use less, mostly around half the dose) are:

- Testosterone derivative (Norethisterone; 5 mg, levonorgestrel; 75 mg) or
- Progesterone- derived progestogens (Cyproterone; 2mg, Medroxyprogeterone; 5mg, cyclogest pessaries; 400 mg, crinone gel; alternate days/ 12 days per cycle) and Spironolactone-derived progestogens (Drospirenone; not active as sequential and use as continuous treatment in 2 mg).

Bleeding problems: if heavy or erratic, the dose of progestogen could be doubled or the duration increased to 21 days. Persistent bleeding beyond 6 months needs investigations.
Side effect of Progesterone include: fluid retention, androgenic side effect in testosterone derivative and mood swing. Natural progesterone has fewer side effects. Drospirenone derivatives recently formulated with low dose estrogen in continuous combined preparation, which progesterone receptors specific, anti-androgenic and anti-meniralo corticoid properties and may have lowering effect on blood pressure.

Estrogen and a lower dose of progesterone also may be given continuously to prevent the regular, monthly bleeding that can occur when combination HRT is used. If the bleeding persisted, the progesterone dose could be doubled or the duration increased to 21 days. Persistent bleeding beyond 6 months needs further investigations.

The current recommendation is to take the lowest dose of hormone therapy for the shortest time possible. Like all prescription medications, HRT should be re-evaluated each year. The combination therapy may be continuous (ie, daily administration of estrogen and progestogen) or continuous sequential (ie, daily administration of estrogen, with progestogen added on certain days).

The following charts list the names of some, postmenopausal hormones.

Estrogen Types:	**Brand Names:**
Pills	Cenestin, Estinyl, Estrace, Menest, Ogen, Premarin
Cream	Estrace, Ogen, Ortho Dienestrol, Premarin
Vaginal ring	Estring, Femring
Vaginal tablet	Vagifem
Patch	Alora, Climara, Esclim, Estraderm, Vivelle-Dot

Progestin Types:	**Brand Names:**
Pills/Capsules	Amen, Aygestin, Curretab, Cycrin, Megace, Prometrium, Provera
Vaginal Gel	Prochieve progesterone gel 4%, 8%

Combination Types:	**Brand Names:**
Pills	Activella, FemHRT, Ortho-Prefest, Premphase, Prempro, low-dose Prempro
Patch	CombiPatch, Climara-Pro

Note: The main drugs which are available in Iraq are Premarine tablet and cream, medroxyprogeterone acetate (provera). Other drugs are not available or available in the private sector on a limited scale .

Androgens:

Women with distressing sexual desire and tiredness should be provided with androgen supplementation. The dose, duration and indication depends on whether the menopause was surgically induced or spontaneous menopause but usually 300mcg of Testosterone patch twice a week could be used.

Risks of HRT:

- Recent analysis of the women's health initiative (WHI) researches shows that: CV risks were confined to the oldest age group, while younger age women show a trend towards improvement of CV risk and significant reduction in all causes of mortality.

- Those studies in addition to the guidance issued by the International Menopause Society, showed that the Risk of breast cancer did not become significant until 7 years after usage (around 1 extra case per 1000 women per annum), and for a woman in a normal menopause, the benefit of HRT far outweigh the risk.

Contraindication to HRT:

- Breast cancer should be regarded as the principle contraindication to estrogen treatment.
- Women with a history of Cardiovascular disorder (CVD) & stroke.
- Recurrent or active blood clots. Venous thromboembolic disease, although transdermal preparations are safer by avoiding first hepatic pass metabolism.
- Natural estrogen when given to normotensive, or hypertensive women, don't cause an elevation in blood pressure and if combined with oral natural progesterone or drospirenone may actually lower blood pressure, so there is little justification from holding HRT in controlled hypertensive women.
- For women seeking HRT with sever endometriosis should be given continuous combined therapy even after hysterectomy to prevent recurrence.
- Known or suspected pregnancy
- Cigarette smokers should consider stopping tobacco use before taking HRT.
- Treatment of patients with endometrial carcinoma is controversial, but there are reports of estrogen use without any detrimental effects in stage I-III disease. Squamous cervical carcinoma is not estrogen sensitive. There are no adverse data in ovarian cancer survivors, although there may be very small risk of ovarian cancer with long term unopposed eostrogen use in healthy women. There are no data for adenocarcinoma of the cervix, vaginal or vulvar cancer.

Duration of therapy:

It is recognized that symptoms often return when HRT is ceased, even after many years of use.

- If the main cause of its use is to improve quality of life, then no dead line could be stated to stop treatment.
- Duration of treatments needs careful judgments of benefits and risks and if therapy needs to be discontinued then that must be done gradually.

Practical prescription advice:

- Still recommended that HRT use mainly for symptoms relieve in short term at a lowest effective dose.
- Considered in long term for prevention of osteoporosis with annual reassessment of risk and advantage.

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4.4.3 Selective ostrogen receptor modulators

Estrogen Agonist/Antagonist (formerly known as SERMs : Raloxifene (Evista) is indicated for reducing the risk of invasive breast cancer in postmenopausal women with osteoporosis. It does not reduce the risk of coronary heart disease. Similar to estrogen, Raloxifene may increase the risk of deep vein thrombosis. It also increases hot flashes and make it worse (which is the main symptom of menopause worsen).

4.4.4 Complementary approach for symptomatic relief

Complementary therapies/ alternatives to HRT:

Now life style changes have been integrated with supplements such as red clover, soy isoflavones can be used for vasomotor symptoms.

Non pharmological alternative: Lubricant gel for vaginal symptoms,

Pharmacological alternatives: Several option can be considered to treat the vasomotor symptoms such as hot flases and night sweats:

1. Fluoxetine and paroxetine are selective serotonin reuptake inhibitors SSRI/ Noradrenaline reuptake inhibitors SNRI: For the treatment of vasomotor symptoms., venlafaxine at a dose of 37.5 mg twice daily.

2. Gabapentin: antiepileptic which can reduce hot flashes at doses of 200 to 1,600 mg/day. Its use is limited because of its side effects.

3. Clonidine is an alpha 2 agonist that is a centrally active α 2 agonist, at a dose of 300-900 mg/day

Comparison of effectiveness reducing hot flashes [2]

Vasomotor symptom reduction with various therapies

THERAPY	% REDUCTION
Hormone therapy	≥ 90%
Venlafaxine	60%–75%
Gabapentin	50%–60%
Selective serotonin reuptake inhibitors (fluoxetine, paroxetine, sertraline)	50%
Vitamin E/soy	25%
Placebo	20%–30%

Other Complementary therapies: phytoeostrogens

Phytoestrogens are estrogens from plants and can be found in foods such as whole grains, dried beans, peas, fruits, broccoli, cauliflower and especially soy products. A diet rich in isoflavones, a type of phytoestrogens, can lower vasomotor menopausal symptoms, CVD, osteoporosis,

[2] Treatment options for menopausal hot flashes. ANDREA SIKON. CLEVELAND CLINIC JOURNAL OF MEDICINE VOLUME 71 • NUMBER 7 JULY 2004. http://ccjm.org/content/71/7/578.full.pdf

breast, colon, endometrial, and ovarian cancer. Effects could be on CV markers as lipid and on arterial compliance and on bone markers/density with possible SERM effect.

4.4.5 Contraception at peri-menopause

The gradual expected changes in fertility and transition into menopause requires special consideration to contraceptive use for this category of women (women aged >40 years).
This part of the guide will discuss the use of contraception for those women, medical criteria for prescription of contraception pre- menopause, when to stop using contraception and the relation of contraception with menopausal symptoms and the use of HRT.

Contraception: Medical Eligibility Criteria (MEC) for women over 40

There are wide ranges of contraceptive methods available, none of which are contraindicated based on age alone. However as individuals get older, age may become a more significant risk factor for developing incidental medical conditions that could impact on contraceptive choice.
A clinical history (medical, sexual, reproductive and social) will enable practitioners to assess the risk of contraceptives as well as the medical and social factors that may influence this use such as frequency of intercourse, menstrual dysfunction and lifestyle factors such as smoking and concurrent medical conditions.

The guidance in the box below provides evidence-based recommendations to clinicians in making decisions about contraceptive choices, including stopping contraception.

Special Considerations for the Contraceptive Method Choice

- Women age 35 and older who smoke—regardless of how much—should not use COCs, the patch, or the vaginal ring.
- Women age 35 and older who smoke 15 or more cigarettes a day should not use monthly injectables.
- Women age 35 or older should not use COCs, monthly injectables, the patch, or the vaginal ring if they have migraine headaches (whether with migraine aura or not).

Health benefits associated with CHC use for women > 40:

Bone health

It is not possible to say, from the evidence that currently exists, whether use of hormonal Contraception influences fracture risk but Women can be advised that

combined contraceptives (COC) use in the perimenopause may help to maintain bone density.

Menopausal symptoms

There is a small amount of data that suggests COC may help to improve some of the symptoms associated with menopause. There may be some theoretical benefit from an extended regimen such as taking three pill packets continuously (tricycling).
In clinical practice CHC may reduce menopausal symptoms and practitioners who are prescribing COC to women aged over 40 years may consider a pill with 30 μg Ethinyl Estradiol as a suitable first choice.

4.4.6 Indications for referral to a higher level of care

The majority of women can be managed in primary care, but in the following situations referral may be necessary for investigation and specialist advice especially about the use of HRT. Referral is indicated in the following conditions:

1. Abnormal Bleeding:
    - Non-HRT users: a sudden change in menstrual pattern, intermenstrual bleeding, post coital bleeding, or post-menopausal bleeding.
    - HRT-users:

      Sequential HRT: a change in pattern of withdrawal bleeds or breakthrough bleeding.

      Continuous combined or long cycle regimens:

        - Breakthrough bleeding persisting for more than 4-6 months after starting or which is not lessening.
        - A bleed after amenorrhea on a continuous combined regimen.
        - Ultrasound scan – ideally transvaginal – reporting endometrial thickness/cervical smear report.

2. Multiple Treatment Failure: Three or more regimens tried. List types of HRT and detail problems.
3. Venous Thrombo-embolism, suspected by Personal history, family history of unprovoked event in a first degree relative age <50 or confirmed cases for investigation and follow up.
4. Premature menopause / Premature Ovarian Failure (Menopause <40).
5. Referral for Ultrasound, Mammogram and Dexa scans when

indicated and as previously mentioned in the guide.

6. Osteoporosis: referral for screening and treatment.
7. Previous or High Risk of Malignancy: e.g. breast± ovarian/ endometrial cancer.

5. Menopause and malignancy

Menopause and cancer risk

A woman who began menopause after age 55 has an increased risk of ovarian, breast, and uterine cancer. This risk is greater if a woman also began menstruating before the age of 12. A woman who menstruates longer than normal during her life is exposed to more estrogen. Excess exposure to estrogen increases a woman's risk of uterine and breast cancers.

Does cancer treatment cause menopause or menopausal symptoms?

Some cancer treatments may cause menopause or menopausal symptoms. Menopause caused by medical treatment is called medical (or surgical) menopause. The symptoms of medical menopause may be worse because the decrease in hormones happens quickly. Even if cancer treatment does not cause menopause immediately, it may cause menopause to start sooner.

The following cancer treatments may cause menopause:

a. ***Oophorectomy (surgical removal of the ovaries).*** This type of surgery is used to treat or prevent ovarian, uterine, and vaginal cancers. It causes menopause immediately because the source of estrogen and progesterone is removed.
b. ***Radiation therapy or chemotherapy.*** Radiation therapy to the pelvis and chemotherapy that damages the ovaries can cause early menopause. Menstrual periods may return for some younger woman after treatment, but women older than age 40 are less likely to have their menstrual periods return.
c. ***Hormonal therapy.*** Hormonal therapy is used to treat breast cancer that is estrogen receptor- and/or progesterone receptor-positive. Hormonal or anti-estrogen therapies include the aromatize inhibitors including anastrozole (Arimidex), letrozole (Femara), exemestane (Aromasin) and tamoxifen.

The drugs tamoxifen (Nolvadex) and raloxifene (Evista) are used to reduce the risk of breast cancer for women who have been treated for breast cancer or who have a higher risk of breast cancer. The side effects of these drugs are similar to the symptoms of menopause.

Can the treatment of menopausal symptoms increase the risk of cancer?

- Women taking combined hormone replacement therapy to manage menopausal symptoms may have increased risk of breast cancer.
- Hormone therapy with estrogen alone is only given to women who have had a hysterectomy because estrogen increases the risk of uterine cancer.

- The Women's Health Initiative also found that women taking combined hormone therapy had a decreased risk of colorectal cancer

- Recent research also showed that women who received combined HRT have a higher risk of dying from non-small cell lung cancer (NSCLC) if they develop the disease. However, woman in the study taking combined HRT therapy were not more likely to develop NSCLC than women who were not taking combined hormone therapy. The study also showed that the risk of dying from lung cancer was higher for women with NSCLC who smoke and take combined hormone therapy.

  Research on combined hormone therapy is controversial and ongoing. The risks and benefits of the treatment are different for each woman.

Breast Cancer

Breast cancer is the most common cancer among women. Hormonal replacement therapy (HRT; estrogen plus progesterone) increases the risk of breast cancer slightly after 5 years of therapy

Ovarian cancer

Ovarian cancer is the fourth leading cause of cancer deaths among women. It most often occurs in women who are older than 50; according to the American Cancer Society, over half of those diagnosed with ovarian cancer are age 60 or older. Risk factors for ovarian cancer include:

- Having a family history of ovarian cancer.
- Having never been pregnant.
- Are over the age of 50 old.

Menopause itself does not cause ovarian cancer. But studies have linked long-term estrogen replacement therapy (more than 10 years) to an increased risk of ovarian cancer. Women should discuss the risks and benefits of this type of hormone therapy with their doctor.

Endometrial Cancer:

It is becoming the most common genealogical malignancy by recent years in developed countries; mainly because of increase life expectancy, obesity & reduction in death from other malignancies. Several observers have suggested that a positive relationship may exist between the occurrence of menopause at an advanced age (>55 years old) and the development of cancer

in the tissues of the female reproductive organs. The incidence of late menopause in cases of adenocarcinoma of the fundus uteri is about four times as high as it is in normal cases. Thus a woman starting to menstruate at the age of twelve and stopping at fifty-four, with a consequent cycle of forty two years, may naturally show a quite different biological reaction of the tissues to estrogenic activity from that of the woman starting at sixteen and ending at forty eight or earlier, with a cycle of estrogenic activity of thirty-two years or less.

Recently, researches reveal that Endometrial Ca at menopause is characterized by being of high grade and poorer prognosis

Cervical cancer:

The second common cancer after breast cancer in females worldwide it's linked to sexual activity especially age at first intercourse.

Vaginal Cancer*:*

Its account for only 1-2% of all gynecological cancers, with a peak incidence the sixth decade of life and mean age of 60-65 years.

Vulvar cancer:

The rarest cancer, account for less than 1% with peak incidence at age of 65 and more. The reactivation risk for human papillomavirus (HPV) infections may increase around age 50 years. Around the world, HPV prevalence spikes among younger women about the time they first have sex, but in Central and South America and Western Africa, a second spike also occurs when women reach menopause, a factor that can increase risk of cervical, vulvar, and vaginal cancers.

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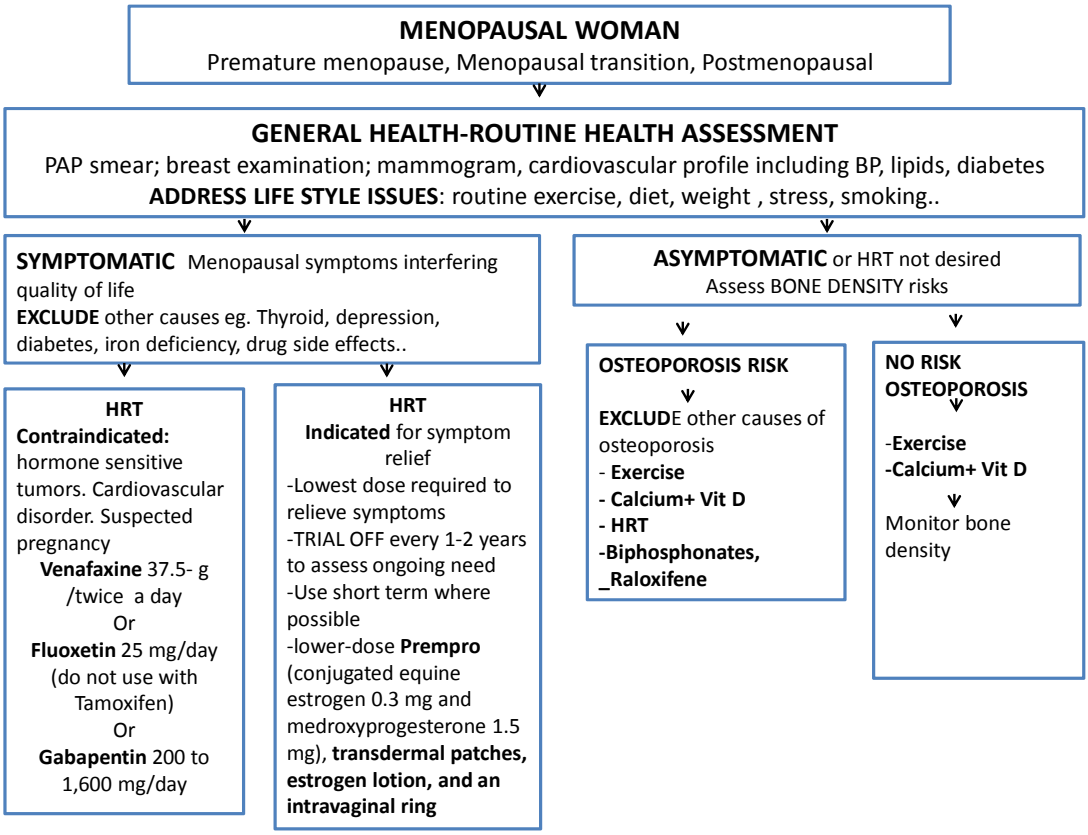
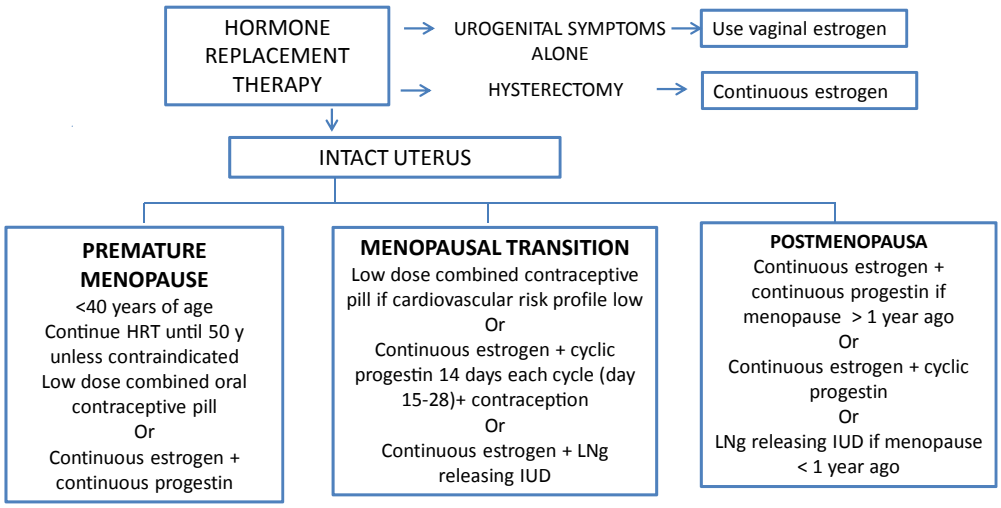
Annex 1: Algorithm for menopause management



Annex 2: Algorithm for HRT



SPECIAL SITUATIONS	
Cardiovascular risks :	Avoid HRT with multiple risk factors, transdermal estrogens if no other options
DVT/Thrombophilia:	Assess baseline risk , family history, previous thrombosis
Cancer:	HRT Contraindicated if breast cancer, endometrial cancer

Annex 3: Performance checklist

- Assess the menopausal symptoms presentation. Normal in woman between 45-55 years. Premature menopause if symptoms appear in younger of 40 years of age. Identification of causes of premature menopause
- Clinical history and determination of risk factors for cardiovascular disorder, smoking and other possible disorders.
- Physical Assessment: weight and determination of BMI, Blood pressure, breast examination.
- Laboratory test: PAP smear, mammogram, cholesterol and lipids, blood glucose.
- Counseling on: changes expected during the menopause and coping mechanisms, nutrition, exercise, weight management.
- Treatment options:
    - Intense menopausal symptoms that interfere with daily activities.
    - Consider Hormonal Replacement Therapy (HRT)
        - lower-dose Prempro (conjugated equine estrogen 0.3 mg and medroxyprogesterone 1.5 mg)
    - Consider alternatives to HRT:
        - Venafaxine 37.5- g /twice a day, or
        - Fluoxetin 25 mg/day (do not use with Tamoxifen), or
        - Gabapentin 200 to 1,600 mg/day
- Osteoporosis prevention:
    - No osteoporosis risk: recommend exercise, Vit D and Calcium
    - Osteoporosis risk: in addition to vit D and Calcium
        - HRT
        - Biphosphonates, _Raloxifene
- Pregnancy prevention. HRT doesn't provide contraception, there is the need to use other methods until at least 12 month since the last menstrual period (Figure 2)
- Follow up every 6 months or earlier if bleeding or other symptoms appeared

Annex 4: General fitness and flexibility exercises for menopause

Gentle exercise that promotes mobility, flexibility and relaxation and at the same time decrease stiffness and soreness often helps the menopausal woman is recommended. Vigor and energy are usually enhanced with regular exercise. Using stairs whenever possible and increasing daily walking time are two of the very best exercises

Deep Abdominal Breathing

This breathing will promote deep relaxation, abundant energy, and stress control: tell the woman to Lie flat on the back with your knees pulled up, keeping your feet slightly apart. Inhale deeply through the nose, allowing your stomach to relax. The stomach should balloon out as you breathe in. Imagine that your body is filling with energy on each inhalation. As you exhale, imagine the air being pushed out from the bottom of your lungs to the top **Joint Flexibility**

Improving range of motion and flexibility in all joints will remedy stiffness and soreness that are so common as we reach menopause.

With the exception of the last one, the following exercises are done in sequence sitting on the floor, legs stretched out in front.

- Toes - Place your hands at your sides and flex your toes 10 times.
- Ankles - Rotate your ankles in each direction 10 times, keeping heels on the floor.
- Knees - Bend the right leg and bring the heel near your buttock. Then lift the right leg off the floor and straighten the right knee, repeating 10 times. Then the left leg and knee 10 times. Next, holding your thigh near your body, rotate your lower leg as you did your ankle, 10 times clockwise and 10 times counterclockwise.
- Hips – Bend the left leg and place your left foot on your right thigh. Hold the left knee with the left hand, and the left ankle with the right hand. Gently move the knee up and down with the left hand; then repeat with the right leg. Now rotate the left knee clockwise 10 times then counterclockwise 10 times. This improves hip flexibility. Repeat with the right knee. Also for hip flexibility, bring the soles of the feet together, bringing the heels close to the body. Using your hands, press your knees to the floor and let them come up again. Repeat 10 times.
- Fingers – Lift your arms to shoulder height. Keeping your arms straight open the hands wide. Flex your fingers, closing over your thumbs. Repeat 10 times.
- Wrists – Flex and extend the wrists, repeating 10 times. Rotate your wrists clockwise and counterclockwise 10 times each. Now hold the hand in extension and move it from side to side at the wrist. Repeat 10 times.

- Elbows – Stretch out the arms at shoulder height with palms facing upward. Bend the arms at the elbow and touch the shoulders with your fingers; then straighten out the arms again. Repeat 10 times with arms front, then with arms extended sideways.

- Shoulders – With arms bent and fingertips touching the shoulders, make circular motions with the elbows. Repeat 10 times clockwise and 10 times counterclockwise.

- Spine – With legs straight out in front, reach over and touch your legs without bending your knees. Repeat 20 times.

- Waist – Stand up and slowly reach over and touch your toes, bending from the waist. Try to keep your knees straight. Repeat 10 times. Remain standing, and spread your legs about 2 feet apart. Bend to the side at the waist first to the left, reaching your right arm over your head, repeating 5 times. Then repeat, bending to the right with your left arm over your head.

Muscle Tension Release, Energy Level Increase

- Legs and pelvis – Stand with legs 2 feet apart and point your feet out at a comfortable angle. Bend your knees slowly and lower your buttocks. Eventually they should be able to go as low as your knees. Move up and down 10 times.

- Legs and pelvis – Stand with legs 2 feet apart and feet facing forward. Rock your pelvis back and forth. Repeat 10 times.

- Legs and pelvis – In the same position, move your hips and pelvis from side to side. Let your torso and arms sway in the opposite direction, as if dancing.

- Entire body – Jump up and down in place for several minutes. Allow your arms to move freely. Shake out your wrists, and raise your arms over your head, while jumping to release tension in the shoulders and arms.

- Shoulders, neck, torso – Sit down with legs out in front. Raise your arms to shoulder level, bending at the elbow. Place your hands on your shoulders with your fingers in front and thumb in back. Turn your elbows, head, and neck to the left and then to the right. Repeat 10 times. Be sure to let your entire torso move with your shoulders and arms. Then move your shoulders in circles in a forward direction 10 times. Repeat in circles in a backward direction 10 times, allowing your torso to follow your shoulders so the movement is fluid.

- Neck and head – Still in a sitting position, flex your neck backward, so that your face looks at the ceiling. Repeat slowly 10 times. Then turn your head from side to side (left to right). Repeat 10 times.

- Eyes – From a sitting position, look straight ahead. Then slowly raise your eyes up and down, then side to side. Repeat 10 times.

Annex 5: Risk factors for breast cancer

Certain risk factors exist,that increase a woman's chance of developing breast cancer

- Age - it's more common in women over 50.
- Family history - if a woman's mother or sister had the disease before menopause, this is occasionally associated with one of two genes linked to breast cancer.
- Previous breast cancer.
- Family history of ovarian cancer.
- Age of pregnancy - women who haven't had children, or whose first child was born after age 30.
- Age of menstruation - starting periods at a young age (under 12 years old).
- Entering menopause later (over age 55) increases breast cancer risks.
- Recent research suggests that women who start smoking regularly within 5 years of the onset of their menstrual periods are 70% more likely to develop breast cancer before the age of 50 than non-smokers.
- Having dense breast tissue.
- Radiation treatment to the chest, especially before 30 years of age.
- Oral contraceptives increase risks slightly, if used over many years.
- Obesity with excess caloric and fat intake.
- Alcohol consumption contributes to the risk of breast cancer.

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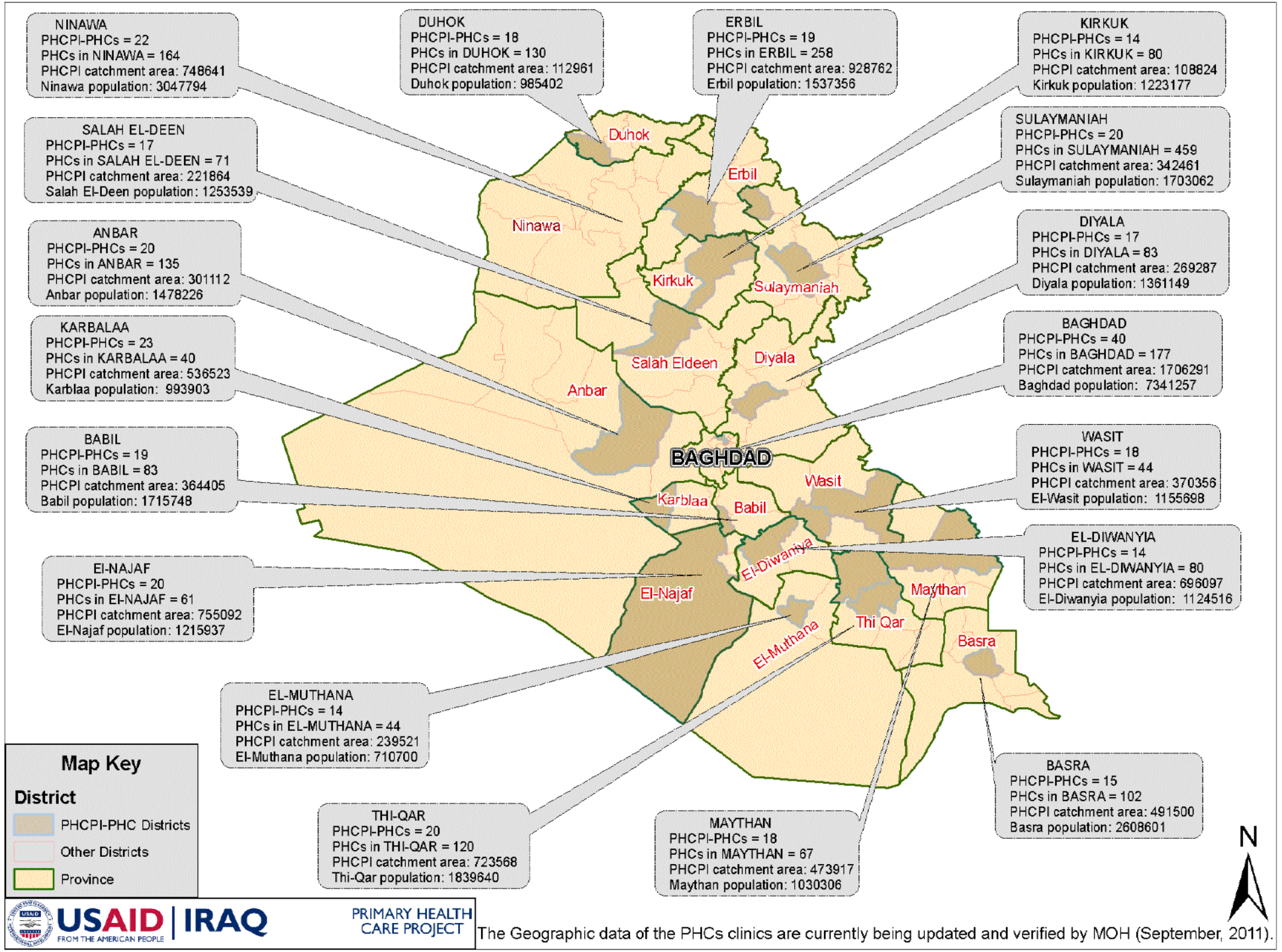
PHCPI-PHCs population mapped to IRAQ population



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PRIMARY HEALTH CARE PROJECT

The Geographic data of the PHCs clinics are currently being updated and verified by MOH (September, 2011).

U.S. Agency for International Development
Primary Health Care Project In Iraq
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