



MenoPro: A Mobile App for Women Bothered by Menopause Symptoms

OVERVIEW OF THE APP AND DECISION-SUPPORT TOOL.

Welcome to MenoPro—your personal guide to managing menopause symptoms. The MenoPro iPhone/iPad app, developed together with The North American Menopause Society (NAMS), is designed to help women work with their health care providers to “personalize” treatment decisions for menopause symptom management. This includes deciding whether prescription medication for management of menopause symptoms would be appropriate and, if so, choosing the optimal treatment. The MenoPro app has two modes: one for women/patients and one for clinicians. Menopause symptoms vary dramatically among women (1,2). Some women have no symptoms as they go through the menopause transition, and other women find that their quality of life is severely affected by hot flashes, night-time sweats, sleep problems, difficulty concentrating, and vaginal dryness. Menopause symptoms are related to the low levels of the hormone estrogen that occur in women when they reach menopause. Some women are good candidates for hormone treatments and others, due to personal choice or risk factors for heart disease, breast cancer, or other conditions, are not appropriate candidates and should consider non-hormone options. One of the most complex health care decisions facing women in midlife is whether to use prescription medications for menopause symptom management, and the menu of treatment options has grown markedly in recent years (2,3). This new app, which can be downloaded free of charge and used on an iPhone or tablet device, helps women work together with their clinicians to individualize treatment decisions, based on the woman’s personal preferences and risk factor status (4-9). The companion free mobile app for clinicians helps you work together and encourages shared decision making.

This new app includes options for “moderate to severe” hot flashes and/or night sweats (defined as bothersome enough to interfere with daily activities, worsen quality of life, and/or interrupt sleep), as well as symptoms including vaginal dryness, pain with sexual activity, or urinary issues. Convenient links provide information about treatment choices, formulations and doses, and “contraindications” (reasons some women should not use a particular therapy). The app calculates a cardiovascular disease (CVD) risk score (risk of heart disease or stroke over the next 10 years) for each woman (10), which is relevant to the decision about starting systemic hormone therapy (HT). Women at high risk of, or with significant concern about, breast cancer may wish to consider non-hormonal therapies. **The tool can be used by women ages 45 years and older with menopause symptoms.** Women who have had removal of both ovaries can use this app at even younger ages. However, women younger than age 45 who are not clearly menopausal, as well as women who have had treatments such as endometrial ablation, progestin-releasing intrauterine device/system, injectable birth control (Depo-Provera), or hysterectomy (surgical removal of the uterus) without removal of the ovaries, may need additional clinical evaluation before using this app (consult your clinician for the laboratory tests that may be most helpful in determining whether you are truly in menopause or have a different condition, such as a thyroid disorder, that is causing your periods to be irregular or absent) (3). The app encourages women to try lifestyle modifications for at least 3 months before beginning HT or other

prescription medications. For information on lifestyle modifications, including something called cognitive-behavior therapy and/or additional remedies, women may find the following link helpful: <http://www.menopause.org/docs/for-women/mnflashes.pdf>. The app also addresses factors that will help you decide on how long to take treatment, including balancing risks of breast cancer, CVD, and thinning of the bones that can lead to fractures (osteoporosis) (1-3). Each step of the decision-making guide should be rechecked at least once every 12 months or if your health status changes.

Background

Women have an increasing number of options, both hormonal and non-hormonal, for the management of menopause symptoms (1-3). A major obstacle to treatment, however, is the complex decision-making process and the lack of good information about available options. This new algorithm (shown in Figure 1) and mobile app for managing menopause symptoms builds on scientific proof and up-to-date research to make the best possible decisions as patients and clinicians share in decision making.

Menopause HT continues to have an important clinical role in the management of hot flashes and other menopause symptoms, but it has both benefits and risks. Although findings from the large Women's Health Initiative (WHI) and other scientific studies have helped to clarify the benefits and risks of HT (4-7), current options include lower doses and medications absorbed through the skin that may further lower risks. Research suggests that individual traits can help to identify women for whom benefits of HT are likely to outweigh the risks (4-9). Age and years since menopause are strong predictors of risks and benefits. Risks of treatment appear to be much lower in younger than older women, particularly those who have had a hysterectomy and require only estrogen treatment (see Figure 2) (4,5). In addition, women with more risk factors for heart attack and stroke, such as abnormal cholesterol levels, obesity, diabetes, metabolic syndrome, or other risk factors, have greater risk of heart attack and stroke while taking hormones than women at lower risk (2-7). These findings have been incorporated into the decision-making process used in this app. Women who are not candidates for HT, or choose not to take HT, can consider and be evaluated for non-hormone treatments. The use of information about risk factors and the personalized risk assessment provided by this app may improve safety and provide a more favorable balance of benefits and risks for both hormone and non-hormone treatments.

Decision-Making Process and Treatment Options

The key elements of the algorithm (Figure 1) include assessment of whether you have bothersome hot flashes (the main reason for starting HT); finding out your personal preference regarding hormone versus non-hormone treatments; seeing whether you have risk factors that would make you ineligible for treatment; taking stock of your years since menopause and baseline risks of CVD, breast cancer, and other health problems; reviewing the benefits and risks of treatment (Figure 2); and, if HT is started, regularly reviewing your need for continued treatment. If hormone treatment is chosen, transdermal is preferable to oral for patients with metabolic syndrome or other significant CVD risk factors. Clinicians may want to begin with lower doses, which are effective for relieving symptoms in many women. In some women, a medication containing conjugated estrogens combined with bazedoxifene (a second agent to protect the uterus) may be an option. A similar process is followed for non-hormone treatments in women who are not candidates for, or who choose not to take, HT. Paroxetine, an antidepressant, prescribed at 7.5 mg per day is an FDA-approved non-hormone medication for vasomotor symptoms; a wide range of other commonly prescribed antidepressants as well as other different medications (gabapentin, pregabalin, and clonidine) can be considered. For women who do not have moderate or severe hot flashes but have significant vaginal dryness or pain with intercourse/sexual activities, without adequate response to vaginal lubricants and/or moisturizers, low-dose vaginal estrogen is an option. Ospemifene, a medication that acts similarly to an estrogen in

the vagina, can also be considered for women without contraindications and who prefer a nonestrogen oral treatment.

Before beginning to use the app, women may want complete the questions in the SELF-ASSESSMENT SECTION, share a summary with their clinician, and review the comments and definitions at the end of that section.

Conclusions

A woman's age, time since menopause, and her risk factor status, as well as the severity of her symptoms, will help to determine whether or not she is an appropriate candidate for prescription medications for menopause symptom management, and this information will lead to a safer and more personalized approach to clinical decision making. Recent research has advanced our understanding of the benefits and risks of available treatment options and enhanced the ability of both patients and clinicians to make informed choices about treatment.

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Disclaimer: This Application is intended for informational purposes only and is not intended as a substitute for professional medical judgment, diagnosis, or treatment. Users of the app are asked to read and accept an End User License Agreement, available on the app.

SELF-ASSESSMENT SECTION (before using the app).

MenoPro is designed to help you decide how to manage your menopause symptoms. Menopause symptoms vary dramatically among women. Some women have few if any symptoms as they go through the menopause transition. [1] Other women find that their quality of life is severely affected by hot flashes, night sweats, and other symptoms. Menopause symptoms are related to the low levels of estrogen in women as they reach menopause. [2] We do not know why symptoms occur in some

women but not others. If you have symptoms that are not clearly associated with menopause, check with your health care provider to be sure there are no other causes of your symptoms.
[Note: Bracketed numbers link to Additional Information]

Let's get started.

What is your age? _____

For information on how age relates to decision-making, tap here [Footnote a]

What was your age when you had your last menstrual period? _____

Questions A: Have you had both ovaries removed?

Yes [Go to Question E]

No [Go to Question B]

Question B: Have your periods become irregular or stopped?

Yes [Go to Question C]

No [You are probably not yet in *perimenopause*, but read more to be sure.] [1]

Question C: Are you younger than 40 years old?

Yes [Go to Question D]

No [Be sure that you are not pregnant. If not, most likely you are entering *perimenopause*. Read more about *perimenopause*. [1] While you are in *perimenopause*, it is helpful to keep a *menstrual calendar*. You can print out a copy of the menstrual calendar. [2] Let's move on to symptoms. [Go to Question E]

Question D: Have you had any of the following: intrauterine device/system, injectable birth control (Depo-Provera), endometrial ablation, hysterectomy, both ovaries removed, chemotherapy, or radiation?

Yes [If you have had one of the procedures or treatments in the list, you might have stopped bleeding as a result of the procedure or treatment. *Read more to find out why*. [3,4]

No [You might be experiencing *early menopause* [4] as a result of *primary ovarian insufficiency*.] [5]

Question E: Is *vaginal dryness/discomfort* your only symptom? [6]

Yes [Go to Question F]

No [Go to Question G]

Question F: Did you have vaginal dryness/discomfort before menopause?

Yes [If the vaginal discomfort is *long standing* or you also had it when you were younger, talk with your provider to help you figure out the cause and possible treatment. *Learn more*.] [7]

No [If your vaginal dryness/discomfort is new since menopause and if you do not have an infection or dermatitis, first-line therapy begins with over-the-counter remedies such as lubricants and moisturizers. For vaginal symptoms caused by sexual intercourse, learn about *over-the-counter remedies* here. [8] If your vaginal symptoms are constant and not caused by sexual activity, please read further [7]

If you have tried over-the-counter remedies without success, see your health care provider to discuss prescription therapies. Learn about *vaginal estrogen options* and a new nonhormonal option called *ospemifene* here. [9] (Also addressed in the app)

Question G: Are you experiencing *hot flashes*, *night sweats*, [10] and/or *other symptoms*? [11]

Yes [Please check all the symptoms you have:]

- Hot flashes (day or night)
- Vaginal dryness
- Pain with sex/intercourse
- Irritability
- Memory, concentration difficulty
- Aching joints
- Moodiness
- Depression
- Sleep disturbances

Next [Go to Question H]

No You are fortunate. Concentrate on staying healthy with a *nutritious diet* [12] and *regular exercise*. [13]

Question H: There are many options for alleviating symptoms of menopause. In addition to staying healthy with a *nutritious diet* [12] and *regular exercise*, [13] four broad categories of approaches have been used by women to manage their menopause symptoms. Read about each one and select the option that seems best suited to you.

- Lifestyle modification [Go to [14]]
- Alternative medicine, over-the-counter therapies [15]
- FDA-approved hormone therapy [16] [If this option is selected, go to Question I]
- Nonhormonal prescription therapies [17]

Question I: Now that you have read about the options, please select the one you favor:

- Lifestyle modification [Go to K]
- Alternative medicine, over-the-counter therapies [Go to K]
- Hormone therapy [If this option is selected, go to Question J]
- Nonhormonal prescription therapies [Go to K]

Question J. You have indicated that you are interested in *hormone therapy* [16] to *relieve all your symptoms*. Please check the box(es) below if you have had or are at high risk for any of the following (discussed further in the app—to be discussed with your health care provider)

- Heart disease
- Blood clots
- High blood pressure
- Stroke
- Breast, endometrial, or ovarian cancer

For more details on reasons why some women should not use HT, click here.[Footnote C]
If yes to any of the above, see your health care provider to discuss your treatment options.
Click *Next* [Go to **K**]

If you have none of the risks listed above, HT may be a good option for your menopause symptoms, and the MenoPro app will help you work together with your clinician to find the optimal treatment, whether hormonal or nonhormonal. If you have had your uterus removed (hysterectomy), you can take estrogen alone. Learn more about hormone options here.[Footnote D].

Although prescription drugs may relieve menopause symptoms, all medications have side effects. Risks of hormone therapy are very small for women in their 50s. For a summary of risks of prescription therapies, click on the following:

Hormone Therapy [Figure 2]

Ospemifene [Footnote b]

SSRIs and SNRIs [Footnote i]

Gabapentin, pregabalin, and clonidine [Footnote j]

Feel free to share a printout of this decision tree with your provider. [Go to **K**]

K: *It may be helpful to print out a summary of your selections for your own records and to discuss with your health care provider.*

Comments and Additional Information

1. *Menopause* is a normal, natural event occurring on average around age 52. Menopause is defined as the final menstrual period and is officially confirmed when a woman has not had her period for 12 consecutive months, unless there are other obvious causes such as surgical removal of the ovaries. Menopause is associated with reduced activity of the ovaries, resulting in lower levels of estrogen, progesterone, and other hormones. It marks the end of a woman's ability to bear children.

Physical clues that you are approaching menopause may start years before your final menstrual period. This time is called *perimenopause* (meaning "around menopause"). It is the result of changing levels of ovarian hormones in your body. Estrogen levels decline, but they do so unevenly. Sometimes they can even be higher than when you were younger. Irregular menstrual periods, hot flashes, vaginal dryness, sleep disturbances, and mood swings are common, normal signs of perimenopause. Heavy or very frequent bleeding is not considered normal and should be discussed with a health care provider.

A few women simply stop menstruating one day and never have another period. However, about 90% of women experience 4 to 8 years of menstrual cycle changes before their periods are gone for good. This time of menstrual cycle changes is known as the *perimenopause transition*. At this time, women may still be able to get pregnant, although this does not happen often. Birth control is advised until 1 year after the last period if pregnancy is not desired.

2. A woman can note her periods on a menstrual calendar to help determine what's normal or abnormal (see www.menopause.org/menocalendar.pdf). Women should consult a health care provider right away if any of the following signs of abnormal bleeding patterns occur:
 - Periods that are extremely heavy, especially if they have not been that way in the past
 - Periods lasting more than 7 days or 2 or more days longer than usual
 - Frequent periods, with intervals shorter than 21 days
 - Spotting or bleeding between menstrual periods
 - Bleeding from the vagina after sexual activity

3. There are several reasons why a woman may stop bleeding. See some of the reasons below:

First and foremost, always be sure pregnancy is not the reason that your periods have stopped.

Intrauterine device/system (IUS)—an IUS that carries a progesterone-like hormone may cause the uterus to stop bleeding without causing menopause. This can also happen with injectable birth

control (Depo-Provera). Estrogen levels will remain normal until a woman reaches her natural menopause.

Endometrial ablation—eliminates the lining of the uterus, which often results in stopping or greatly reducing most uterine bleeding without causing menopause. Estrogen levels will remain normal until a woman reaches her natural menopause.

Hysterectomy—having the uterus removed stops all uterine bleeding without causing menopause, unless both ovaries are removed. Estrogen levels will remain normal or near normal until a woman reaches her natural menopause.

Both ovaries removed—having had both ovaries removed will cause menopause even if the uterus is not removed because the ovaries are the source of estrogen. A woman with both ovaries removed can start bleeding again if she uses HT.

Chemotherapy and radiation—both of these treatments can result in temporary or permanent menopause. Talk with your oncologist about the possible effect of your treatment on menopause.

4. *Early menopause* refers to menopause before the age of 40. It can occur when medical treatments such as chemotherapy or radiation damage both ovaries or when a woman has both ovaries removed surgically. It can also be caused by a condition called *primary ovarian insufficiency* (POI) [5]. Because women with early menopause will be without estrogen much longer than other women, they should talk with their provider about HT or hormonal contraception to treat their symptoms and reduce bone loss until the average age of menopause, as long as there is no reason they should avoid hormones (51). Hormone therapy may not be appropriate for women who have had breast, endometrial (uterine), or ovarian cancer.
5. POI is a condition in which younger women (sometimes as young as their teens) only have occasional periods or no periods, signifying a decreased number of eggs in their ovaries. Ovulation may still occur, so pregnancy is possible. Some women with POI have typical menopause symptoms, while others do not. Some women resume normal periods, but early menopause also is possible.
6. Bothersome symptoms of the vagina and vulva (outer lips of the vagina) are common in women of all ages, but they increase with menopause. The decrease in estrogen with menopause is a major contributor to vaginal dryness, itching, burning, discomfort, and pain during intercourse.
7. For distressing vaginal symptoms that are long-standing, the causes can include such conditions as *vestibulodynia* (also called vulvar vestibulitis or vulvodynia), recurrent yeast infections, allergic reactions, and certain skin conditions. If you had difficulty tolerating tampons or pelvic examinations with a speculum, there may be other reasons for your vaginal discomfort besides menopause. It is important to discuss this symptom with your health care provider.
8. For symptoms of vaginal dryness/discomfort, over-the-counter remedies include:
 - *Vaginal lubricants* reduce discomfort with sexual activity when the vagina is dry by decreasing friction during intercourse. These products can be used on men or women, depending on preference. If your vagina is irritated by the product, stop using it and try a different product.
 - *Vaginal moisturizers* line the wall of the vagina and maintain vaginal moisture. They are used at times other than intercourse. As with your face or hands, regular use of the moisturizer may provide better results.
 - Many brands and formulations are available. If you are not satisfied with the results, see your health care provider to discuss the option of low-dose vaginal estrogen. [10]

9. Low-dose vaginal estrogen is an effective treatment for vaginal symptoms related to menopause. It is applied directly to the vagina to increase the thickness and elasticity of vaginal tissues, restore a healthy vaginal pH, increase vaginal secretions, and relieve vaginal dryness and discomfort with sexual activity. Women who have had breast, endometrial (uterine), or ovarian cancer should consult their oncologist before using estrogen therapy. There are three main types of vaginal estrogen:

- a. *Vaginal creams*: vaginally inserted once daily for 2 weeks, then 2 or 3 times weekly
- b. *Vaginal ring*: placed in the vagina every 90 days
- c. *Vaginal tablet*: inserted into the vagina once daily for 2 weeks using a slender disposable applicator, followed by one tablet twice weekly.

The FDA has also recently approved ospemifene (a nonestrogen oral product) for treatment of the genitourinary symptoms described above. Ospemifene also should not be used in women with unexplained vaginal bleeding or known or suspected breast cancer, endometrial cancer, or other estrogen-dependent tumors. It also should not be used in patients with past or current venous or arterial disease. For even more information about vaginal symptoms due to menopause, [click here](#). [Footnote B]

10. More than 75% of North American women have hot flashes during perimenopause and for years after menopause onset. Hot flashes are thought to be the result of changes in the hypothalamus, the part of the brain that regulates the body's temperature. The hypothalamus senses that a woman is too warm and starts a chain of events to cool the body down. Blood vessels near the surface of the skin dilate (enlarge) so blood flows there and gives off body heat. This produces a red, flushed look to the face and neck in light-skinned women.

Hot flashes that occur at night are called night sweats because many women wake up with their nightclothes and hair damp or wet. Night sweats can interfere with sleep, even if they are not strong enough to wake you up. Although it's commonly said that menopause makes women irritable, sleep disturbances cause fatigue, which can also lead to irritability.

11. During perimenopause, some women are bothered by other symptoms such as moodiness, irritability, difficulty concentrating, and aching joints, which may or may not be related to menopause. Some women may also experience true depression at this time in life. Although some moodiness and irritability may improve with HT, true depression should be treated with counseling and/or antidepressants. See your health care provider if you think you might have depression. Women who have had depression in the past may be more vulnerable to a recurrence around the time of menopause.

12. A nutritious diet low in saturated and trans fats and in simple carbohydrates (refined flour, sweets, potatoes, white rice) and high in whole grains, fruits, legumes (beans), and vegetables, with adequate water, vitamins, and minerals, is vital to good health. Protein should be in the form of beans, low-fat meats and fish, dairy (if not lactose intolerant), and eggs.

13. Regular exercise is an important part of daily life. Physical inactivity is a risk factor for many serious diseases. Some activities that help the heart, bones, muscles, balance, body weight, mood, and one's overall sense of well-being include brisk walking, running, aerobics, dancing, tennis, weight training, and yoga.

14. Although the following lifestyle approaches have not been subjected to rigorous scientific study, they will do no harm, cost little or nothing, and may offer relief for some hot flashes:

- Identify and avoid personal hot flash triggers. These could include external heat (such as a warm room or using a hair dryer), stress, hot drinks, hot or spicy foods, alcohol, caffeine, and cigarette smoking.
- Try out meditation, yoga or tai chi, qigong, biofeedback, positive visualization, acupuncture, or massage.
- Try to stay cool during the day and while sleeping.
- Take slow, deep, abdominal breaths in through the nose and release them out through the mouth at the beginning of a hot flash.
- Try to lose weight, which may help relieve hot flashes in overweight women.
- Try meditating several times a day.

15. Some women find relief for hot flashes with alternative, over-the-counter remedies such as dietary supplements, but most scientific studies do not support their use:

- Isoflavones (weak, plant-derived estrogens), most commonly found in soy foods but also in dietary supplement pills, have been found to reduce mild hot flashes in some studies. Eating one or two servings of soy foods daily may provide greater benefits than supplements. An effect on hot flashes, if any, may take weeks. There is some controversy about whether breast cancer survivors should use isoflavones.
- In some studies, a brand of dietary supplement pill made in Germany containing the herb black cohosh decreased hot flashes, but research has not been consistent. Women with liver problems should not take this herb.
- Over-the-counter cooling gels applied during a hot flash are sometimes helpful.
- Acupuncture has decreased hot flashes in some women but not all of them.
- Hypnosis has been found to decrease hot flashes in some women.
- In most cases, alternative therapies have not been found to reduce hot flashes as well as estrogen or other prescription medications, but some women are satisfied with the improvement they get.

16. HT is the most effective treatment for menopause symptoms. Recently, low-dose paroxetine mesylate (a nonhormonal prescription medication) has also been approved by federal regulatory agencies in the United States and Canada for treating menopause symptoms [see 18]. HT encompasses both estrogen-alone therapy (ET) and estrogen-progestogen therapy (EPT).

- *ET* is prescribed for women who have had a hysterectomy.
- *EPT* is prescribed for women with a uterus as protection against uterine cancer, which can be caused by use of estrogen alone.

HT can be delivered to the body in a number of ways: pills, skin patches, skin gels, skin sprays, and vaginal preparations. There are many different doses, and even vaginal estrogen can treat hot flashes if the dose is high enough.

- a. Oral tablets are the most commonly prescribed preparation in North America. These preparations circulate through the body after being absorbed from the gastrointestinal tract and passing through the liver.
- b. Transdermal estrogen (such as skin patches, gels, emulsions, and sprays) deliver estrogen through the skin into the bloodstream. These preparations can be taken in lower doses than oral tablets because they do not have to be absorbed by the gastrointestinal tract.
- c. Some studies suggest that transdermal estrogen may carry a lower risk of blood clots than oral ET.

- d. HT also helps to protect your bones from osteoporosis while it is treating your menopause symptoms.
- e. Other risks and benefits: See Figure 2 above.

Risks: small increased risk of stroke, gallbladder problems, breast tenderness, and urinary incontinence with systemic HT. Risk of heart disease may be higher in older women who use HT. Risk of breast cancer was increased with EPT but not with ET.

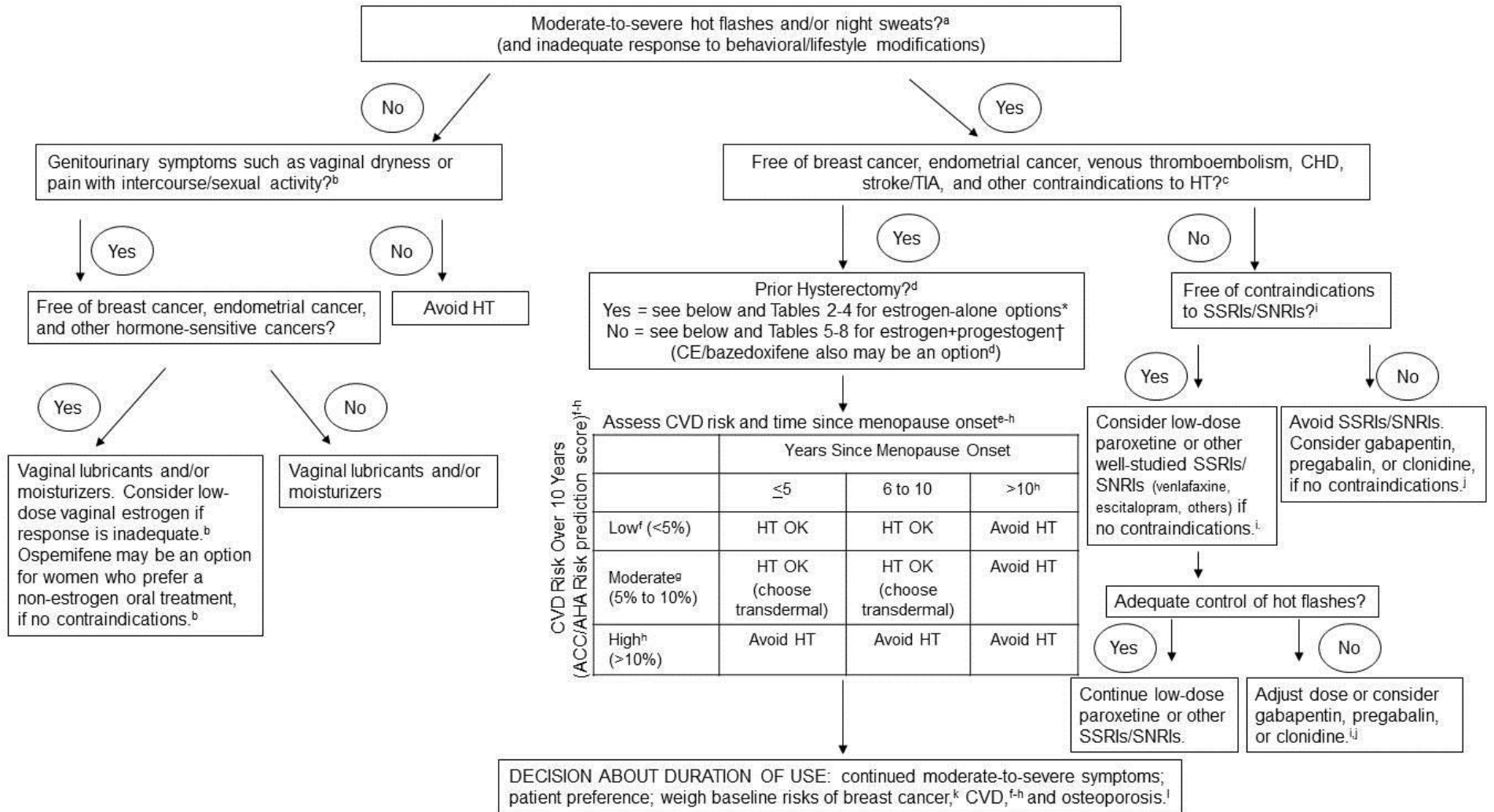
Benefits: overactive bladder may improve with vaginal estrogen; joint pain is better for some women; moodiness and sleep may improve; and decreased risk of fracture and diabetes.

Other prescription hormonal treatments for hot flash relief for women who cannot use (or choose not to use) estrogen include progestin-only contraceptives, other progestins such as medroxyprogesterone acetate or megestrol acetate, and oral progesterone.

- 17. Paroxetine mesylate is an FDA-approved nonhormonal treatment for hot flashes. Other SSRIs/SNRIs, gabapentin, pregabalin, and clonidine may be additional non-hormonal options. These and other treatment options are addressed in the MenoPro app.

START the MenoPro app now for menopause symptom decision making and deciding among the hormonal and non-hormonal treatments.

Figure 1. Algorithm for Menopausal Symptom Management and Hormonal/Non-Hormonal Therapy Decision Making.



Footnotes to Algorithm and Supplemental Tables (Note: these footnotes are intended primarily for health professionals and include technical language):

Footnotes to Algorithm and Supplemental Tables:

Abbreviations

HT = menopausal hormone therapy; FDA= Food and Drug Administration; NAMS=North American Menopause Society; CHD=coronary heart disease; TIA=transient ischemic attack; ASCVD= atherosclerotic cardiovascular disease; CVD=cardiovascular disease; ACC/AHA= American College of Cardiology/American Heart Association; ET=estrogen therapy; EPT=estrogen+progestogen therapy; CE=conjugated estrogens; SSRI=selective serotonin reuptake inhibitors; SNRI= serotonin/norepinephrine reuptake inhibitors; hCG=human chorionic gonadotropin; FSH=follicle stimulating hormone; TSH=thyroid stimulating hormone; PRL=prolactin.

- a MenoPro applies to women with menopause symptoms who are 45 years of age and older. It also can be used for women who have had both ovaries removed, regardless of age. Women younger than age 45 or those women not clearly menopausal may need certain blood tests before using MenoPro. Blood tests may include HCG, FSH, TSH, PRL, and other tests (3). “Moderate-to-severe hot flashes and/or night sweats” are bothersome symptoms that interfere with daily activities, impair quality of life, and/or interrupt sleep. Patients should try lifestyle modifications before using this algorithm (TAP HERE to see or print out lifestyle modification guidelines for the patient: <http://www.menopause.org/docs/for-women/mnflashes.pdf>). For any medications prescribed, women should read the product information sheet to know the current benefits and risks.
- b Women who have vaginal dryness or pain with intercourse or other sexual activities, without bothersome hot flashes, may be candidates for low-dose vaginal estrogen or other treatments. TAP HERE to see Table 1 for vaginal estrogen options. Contraindications for vaginal estrogen include unexplained vaginal bleeding and known or suspected breast or endometrial (uterine) cancer or other estrogen-dependent tumors. Ospemifene may be an option for women who prefer a nonestrogen oral treatment. Contraindications for ospemifene include all of those for vaginal estrogen (above), as well as blood clots in the legs or lungs, other clotting problems, heart attack, stroke, other blood vessel diseases, severe liver disease, or use of estrogens or estrogen agonists/antagonists. Women should be evaluated on an ongoing basis for genitourinary symptoms, regardless of other treatments. Read more about these symptoms at: <http://www.menopause.org/docs/for-women/mndryness.pdf>.
- c For women interested in considering HT, contraindications should be assessed. TAP HERE to see contraindications/cautions: unexplained vaginal bleeding; liver disease; blood clots in the legs or lungs; known blood clotting disorder; untreated hypertension; history of breast, endometrial (uterine) cancer, or other estrogen-dependent tumor; known hypersensitivity to HT, or history of heart attack, angina, coronary bypass surgery, angioplasty/stent, stroke, or TIA. Women with one or more 1st degree relatives with breast cancer (BC) or otherwise at increased risk of BC (see Gayle Risk Score at <http://www.cancer.gov/bcrisktool/>) may want to consider non-hormonal therapy. For other contraindications, including high triglycerides or gallbladder disease, oral estrogen should be avoided, but transdermal estrogen may be an option. Transdermal estrogen also may be less likely to reduce libido than oral estrogen. Women taking thyroid medication may need dose adjustments after starting or stopping HT.
- d Women with hysterectomy are candidates for ET (TAP HERE to see Tables 2-4 for oral and transdermal ET options). Women with an intact uterus should take combination EPT (TAP HERE to see Tables 5-8 for EPT options). FDA-approved bioidentical ET and EPT options are shown in

Table 9 (TAP HERE), and pros and cons of different routes of administration of HT are shown in Table 10 (TAP HERE). CE/bazedoxifene (CE with a third-generation selective estrogen receptor modulator) is an additional FDA-approved option for women with an intact uterus, especially those with concerns about breast tenderness, breast density, or uterine bleeding (TAP HERE); the contraindications are the same as for systemic HT (and/or hypersensitivity to its ingredients). Costs of products have a wide range.

e Reassess each step at least once every 6 to 12 months (assuming patient's continued preference for HT) or if patient's health status changes. If no symptom relief within 3 to 6 months, adjust dose or change to different treatment. For duration of treatment decisions, see NAMS HT Position Statement: <http://www.menopause.org/docs/default-document-library/psht12.pdf?sfvrsn=2> and Kaunitz AM. *Menopause*: June 2014: <http://www.menopause.org/docs/default-source/2013/nams-practice-pearl-extended-ht-duration.pdf>. Also see footnotes k and l.

f ,g, and h **Ten-year risk of CVD, based on the ACC/AHA ASCVD Risk Estimator**
www.imedicalapps.com/2014/04/ascvd-risk-estimator-app/
Source: Goff DC, et al, *Circ* 2013 (reference 10)

Enter information on age, race/ethnicity, smoking, diagnoses of hypertension, diabetes, and/or high cholesterol: a preliminary estimate of your 10-Year atherosclerotic CVD (ASCVD) Risk Score is calculated: _____

(Your clinician will help you to calculate a more detailed CVD Risk Score. In the meantime, your risk can be estimated as follows: if you have 3 or more of the following risk factors [smoking, hypertension, high cholesterol, diabetes] or diabetes plus 1 other risk factor, the preliminary risk estimate would be in the High category below; if you have 2 of these risk factors or diabetes alone, the preliminary risk estimate would be in the moderate category below; and if you have 0 or 1 risk factor and no diabetes, the preliminary risk estimate would be in the low-risk category below.)

Enter number of years since last menstrual period: _____

___ **Low^f (<5%) 10-Year CVD Risk and less than 10 years since menopause:** Patient appears to be a candidate for either oral or transdermal therapy. Women with hysterectomy can take ET (see footnote d and TAP HERE for options and dosages). Women with an intact uterus on HT should take EPT (TAP HERE for options and dosages). FDA-approved bioidentical options (TAP HERE) and pros/cons of oral versus transdermal estrogen (TAP HERE) are summarized. Go to footnotes k and l regarding duration of treatment. CE/bazedoxifene (a third-generation SERM) is an additional FDA-approved option for women with an intact uterus (dosing: CE 0.45 mg; bazedoxifene 20 mg daily) (TAP HERE).

___ **Moderate^g (5%-10%) 10-Year CVD Risk and less than 10 years since menopause:** Patient should avoid oral estrogen, but transdermal estrogen may be an option because it has a less adverse effect on clotting factors, triglyceride levels, and inflammation factors than oral estrogen (TAP HERE to see transdermal options and dosages). (TAP HERE to see pros/cons of oral vs transdermal estrogen.) (TAP HERE to see FDA-approved bioidentical options.) Go to footnote k and l regarding duration of treatment.

^gWomen with obesity, diabetes, or metabolic syndrome and otherwise considered to be candidates for HT may do better with transdermal than oral estrogen (TAP HERE to see definition of MetS). Metabolic syndrome is defined as the presence of three or more of the following criteria in women: 1) abdominal obesity (waist circumference >35 in [88 cm]); 2) triglycerides ≥150 mg/dL (1.69 mmol/L); 3) high-density lipoprotein cholesterol <50 mg/dL (1.3 mmol/L); 4) blood pressure ≥130/≥85 mmHg;

and 5) fasting glucose ≥ 110 mg/dL (6.1 mmol/L) (Adult Treatment Panel III National Cholesterol Education Program 2010).

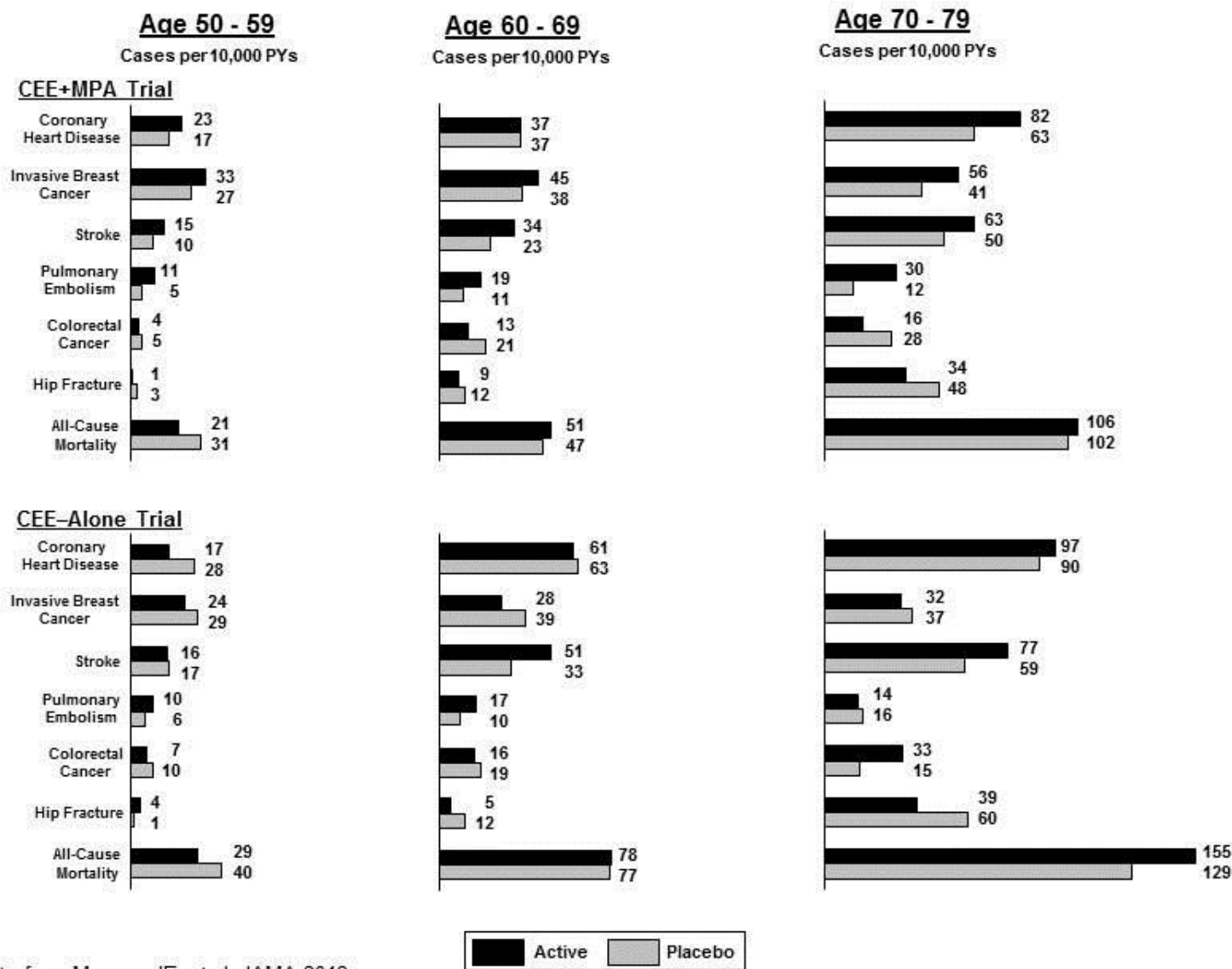
___ **High^h (>10%) 10-Year CVD Risk:** Patient should avoid initiation of systemic HT. Go to footnote i for nonhormonal treatment options. If the patient has genitourinary symptoms, she may be a candidate for low-dose vaginal estrogen or other treatments (go to footnote b).

^hWomen >10 years past menopause also are generally not good candidates for starting (first use of) systemic HT (go to footnote b and i). However, decisions about starting or continuing systemic HT beyond age 60 or more than a decade past menopause (or restarting HT in prior users) require individualized decision making and consideration/discussion of the benefit:risk balance (see footnote k and l).

- i TAP HERE to see contraindications to SSRIs/SNRIs: hypersensitivity or adverse drug reaction on these medications, neuroleptic malignant syndrome, serotonin syndrome, and concurrent use of MAO inhibitors. SSRIs/SNRIs should be used with caution in patients with bipolar disease, uncontrolled seizures, severe liver or kidney disease, uncontrolled hyponatremia, concurrent use of other SSRIs/SNRIs, or poorly controlled hypertension. May increase suicidal thoughts within the first few months of treatment, although observed primarily in youth and young adults. Preliminary evidence suggests an increase risk of bone fractures. (TAP HERE for Paroxetine dosage and other information) Paroxetine 7.5 mg/d (Brisdelle, which contains paroxetine mesylate) is the only SSRI/SNRI currently approved by FDA for treatment of moderate to severe vasomotor symptoms. Paroxetine and other potent hepatic isoenzyme CYP2D6 inhibitors (eg, fluoxetine, duloxetine) should be used with caution in women on tamoxifen due to potential reduction in effectiveness of tamoxifen. (TAP HERE for information on other SSRIs/SNRIs) (off-label use): venlafaxine 75-150 mg/d; escitalopram 10-20 mg/d; citalopram 10-30 mg/day; desvenlafaxine 50 mg/d; paroxetine hydrochloride 10-20 mg/day; paroxetine CR 12.5-25 mg/day; others (similar contraindications). Dosages may need to be adjusted. For severe and resistant symptoms, other less well-established treatments (eg, high-dose progestin, stellate ganglion blockade) may be options.
- j TAP HERE for contraindications to and dosing of gabapentin, pregabalin, and clonidine (off-label use): Gabapentin and pregabalin are contraindicated in patients who have demonstrated hypersensitivity to the drugs or their ingredients. Caution: anticonvulsants may increase suicidal thoughts and behaviors and cause drowsiness and dizziness and impair balance and coordination. Gabapentin and pregabalin should be dose adjusted in patients with kidney disease. Pregabalin may impair memory and concentration. Clonidine is contraindicated in patients with demonstrated hypersensitivity or low blood pressure and may cause lightheadedness, hypotension, headache, and constipation; sudden cessation of treatment can be associated with significant rise in blood pressure. Dosing: gabapentin 900-2,400 mg/d (dose divided 3 times/d); pregabalin 150-300 mg/d (dose divided twice per day); clonidine 100 μ g/day. (Dosages may need to be adjusted.)
- k and l TAP HERE to see information on duration of ET in a patient with hysterectomy and HERE to see information on duration of EPT in a patient with an intact uterus. Decisions about duration of treatment should be individualized and will depend on a number of factors, including patient preference for continuing treatment, persistence of moderate to severe menopause symptoms, and the patient's underlying risk of breast cancer, CVD, osteoporotic fracture, and other conditions. Several other tools, including the Gail Score Estimator for Breast Cancer Risk (<http://www.cancer.gov/bcrisktool/>) and the Fracture Risk Assessment Tool (FRAX; at <http://www.shef.ac.uk/FRAX/tool.aspx?country=9>), may be helpful for these assessments. NAMS generally recommends treating for the duration of time consistent with treatment goals but avoiding durations longer than 7 years for ET and 5 years for EPT (NAMS HT Position Statement: <http://www.menopause.org/docs/default-document-library/psht12.pdf?sfvrsn=2>). However, extended duration treatment may be appropriate in selected patients, such as women at low risk of breast

cancer and CVD but at elevated risk of fracture, or patients at low risk who have tried to discontinue treatment but have return of significant symptoms (see below for further discussion: <http://www.menopause.org/docs/default-source/2013/nams-practice-pearl-extended-ht-duration.pdf>).

Figure 2. WHI Hormone Therapy Trials: Absolute Risks (cases per 10,000 person-years) for Outcomes in the Intervention Phases of the Estrogen-Progestin and Estrogen-Alone Trials, by Age Group



Source: Data from Manson JE, et al. JAMA 2013.

Resources and Tables Included in the App

Summary of lifestyle modifications that can be tried for at least 3 months before considering pharmacologic therapy for vasomotor symptoms: NAMS' MenoNotes on hot flashes (<http://www.menopause.org/docs/for-women/mnflashes.pdf>). Clinician may want to print this out for, or send by email to, the patient as a handout.

NAMS Hormone Therapy Position Statement, 2012: available at:
<http://www.menopause.org/docs/default-document-library/psht12.pdf?sfvrsn=2>

Personalized Estimation of the 10-Year Atherosclerotic Cardiovascular Disease Risk Score from the American College of Cardiology/American Heart Association (ACC/AHA ASCVD Risk Estimator)
<http://www.imedicalapps.com/2014/04/ascvd-risk-estimator-app/>
Source: Goff DC, et al, *Circulation* 2013 (reference 10 above)

Figure displaying absolute risks of chronic disease outcomes by age group, Women's Health Initiative Hormone Therapy Trials: data from Manson JE, et al. *JAMA* 2013;310:1353-1368 (reference 4 above).

NAMS Practice Pearl on Extended Duration Use of Hormone Therapy: Kaunitz A. (available online at: <http://www.menopause.org/docs/default-source/2013/nams-practice-pearl-extended-ht-duration.pdf>)

Several tables adapted from *Menopause Practice: A Clinician's Guide*, 5th edition, NAMS, 2014, * including:

Table 1. Vaginal Estrogen Therapy Products for Postmenopausal Use in the United States and Canada (detailed listing of products, composition, and dosages)

Table 2. Oral Estrogen Therapy Products for Postmenopausal Use in the United States and Canada (detailed listing of products, composition, and dosages [categories of low, moderate, and high])

Table 3. Transdermal Estrogen Therapy Products for Postmenopausal Use in the United States and Canada (patches, gels, emulsions, and sprays: detailed listing of products, composition, and dosages [categories of low, moderate, and high])

Table 4. Approximate Equivalent Estrogen Doses for Postmenopausal Use (oral, transdermal, and vaginal formulations)

Table 5. Combination Estrogen-Progestogen Therapy Products for Postmenopausal Use in the United States and Canada (*oral continuous-cyclic, oral continuous-combined, oral intermittent-combined, and transdermal continuous-combined regimens*)

Table 6. Progestogens Available in the United States and Canada (Detailed listing of products, composition, and dosages)

Table 7. Estrogen-Progestogen Therapy Regimens, Terminology (sequential, continuous-combined, intermittent-combined)

Table 8. Minimum Progestogen Dosing Requirements for Endometrial Protection With Standard Estrogen Dosing

Table 9. FDA-approved "Bioidentical" Hormone Products (FDA-approved products containing estradiol and/or progesterone)

Table 10. Pros and Cons of Hormone Therapy Routes of Administration (oral, transdermal, vaginal)

*Note that information on hormone therapy formulations and dosages is regularly updated on the NAMS website at: <http://www.menopause.org/docs/default-source/2014/nams-ht-tables.pdf>).

Algorithm is adapted from: Manson JE, Bassuk SS. The menopause transition and postmenopausal hormone therapy. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. Harrison's Principles of Internal Medicine. New York: McGraw Hill; 2011; NAMS Hormone Therapy Position Statement 2012: <http://www.menopause.org/docs/default-document-library/psht12.pdf?sfvrsn=2>); Menopause Practice: A Clinician's Guide, 5th edition, NAMS 2014; and NAMS website listing of available therapies (<http://www.menopause.org/docs/default-source/2014/nams-ht-tables.pdf>).
