Putting the latest data into practice:
Case studies and clinical considerations
in menopausal management

Dr. Holly Thacker: In light of the updates that Drs. Hodis and Gass have presented on hormone therapy (HT) for menopausal women and that Drs. Jenkins and Sikon have presented on nonhormonal options for menopausal management, let’s start our roundtable by considering a couple of case studies that will give us the chance to apply the latest data in a practical way.

■ CASE 1: A SYMPTOMATIC 67-YEAR-OLD IN WHOM HORMONE THERAPY WAS ABRUPTLY STOPPED

Dr. Margaret McKenzie: A 67-year-old menopausal woman presents for the evaluation of hot flashes, vaginal dryness causing dyspareunia, and decreased libido. She was previously on estrogen-progestogen therapy (EPT), consisting of daily conjugated equine estrogens and medroxyprogesterone acetate, for 15 years starting at the time of natural menopause. Her gynecologist discontinued this HT abruptly at the time of the initial release of data from the Women’s Health Initiative trial, and the patient is now seeking another opinion about resuming HT. When she presents, she has been off HT for less than 6 months. Would you restart HT in this patient?

Dr. Andrea Sikon: The abrupt discontinuation certainly contributes to her symptoms. The short duration of time off HT is important, and would lead me to restart HT after an updated review of risk factors. She had been on it for 15 years and has done fine, so she appears to be an ideal candidate to restart.

Dr. McKenzie: What specific questions would you ask when doing your risk assessment? How would you evaluate this patient to determine whether she is a good candidate to continue HT?

Dr. Thacker: I would obtain a family history. Using a population-based risk assessment such as the Gail model, I would calculate her absolute risk of breast cancer based on her duration of EPT use. I might offer her a lower-dose regimen. A conjugated equine estrogen dosage of 0.3 mg/day may be as effective in a 67-year-old woman as 0.625 mg/day is in a younger woman in terms of relieving vasomotor symptoms, depending on individual metabolism. We do have evidence from the HOPE trial that 0.3 mg/day is effective for relief of vasomotor symptoms. In addition, data from the Nurses’ Health Study show no increased risk of stroke with 0.3 mg/day, as opposed to the increased risk with 0.625 mg/day, and there are other data showing that the risk of stroke is possibly related to dosage.

At the same time, we do not yet have long-term data to show that the lower dose is necessarily safer and we do not have data on bone fracture risk with the lower dose, so I would want to know this patient’s bone mineral density (BMD). I would also want to know about her cardiovascular risk profile, including...
her lipid profile, and I would want more details about her sexual function.

**Dr. McKenzie:** I will supply a few more case details. This patient’s body mass index (BMI) was 24 kg/m². She exercised regularly. Her BMD was normal for her age. She was taking a statin to treat hyperlipidemia. She was a nonsmoker, and her family history was unremarkable. Does any of this information change the way that you would counsel her?

**Dr. Howard Hodis:** Knowing her BMI and that she was on a statin, I would have even less of a problem reinitiating HT.

**Case continued**

**Dr. McKenzie:** Well, EPT was reinitiated in this patient at a lower dose (0.45/1.5 mg), and she was satisfied. At her most recent visit, several years later, the possibility of reducing her dose of HT was offered; however, the patient is happy with her quality of life and accepts whatever risk that continued HT may bring. She inquired about transdermal testosterone to restore her sex drive, and it was agreed that if it receives US marketing approval for women with decreased libido, a 24-week trial would be attempted.

**Dr. Hodis:** If you look at the data, this patient not only may enhance her quality of life by continuing HT but might extend it as well.

**Dr. Thacker:** Many patients inquire about using testosterone only, without estrogen, for treating dyspareunia and low libido. Clinicians must understand that testosterone is aromatized to estrogen. If a patient is on a high dose of oral estrogen, I would consider switching to transdermal estrogen before trying testosterone, whose use in women remains off-label in the United States. But the patient in our case has been doing well for several years on low-dose estrogen and she still has her ovaries.

**Dr. Margery Gass:** Some colleagues and I completed a study, which was presented at a recent Endocrine Society meeting, in which transdermal testosterone was just as effective without estrogen in increasing libido. But this remains moot for general clinical practice unless the transdermal testosterone patch is approved in this country (as it is already approved for use in women in Europe).

**Dr. Hodis:** Would any of you be worried about this patient’s fracture risk after having HT stopped following 15 years of use? Data show that the rate of bone loss after abrupt cessation of HT is just as great as when a woman is going through menopause.

**Dr. Gass:** Yes, and that is exactly the point. The woman should be assessed under these circumstances just as she would be at menopause, using the same risk factors.

**Dr. Thacker:** I think that underscores that there is risk in stopping treatment, just as there is in taking treatment or not taking treatment, and all of these risks should be considered. Many times, once a patient is off HT, some clinicians forget to check the patient’s BMD or to do a complete genital examination.

**Dr. Sikon:** Many providers who do not specialize in women’s health may forget that when HT is stopped, it is as if a newly menopausal state is being created. Providers need to think about ensuing changes in bone and genitourinary status as well as quality-of-life concerns.

**Dr. McKenzie:** In today’s clinical environment, there is awareness of the importance of long-term bone health because patients are living longer. The use of BMD measurements in practice is clearly expanding.

**Dr. Thacker:** It is worth noting that all of the drugs used to treat osteoporosis have been studied primarily in women who already have osteoporosis. The therapy with the most data to support a reduction in the risk of all types of fracture is HT. These data are very impressive, and although fracture prevention would not be the sole reason for using HT, it can make the overall risk-benefit assessment easier, particularly if it can be determined whether or not an individual patient is at high risk of venous thromboembolism (VTE).

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**CASE 2: A SYMPTOMATIC 47-YEAR-OLD WITH A HISTORY OF BREAST CANCER**

**Dr. McKenzie:** A 47-year-old postmenopausal woman with a 7-year history of breast cancer presents for the management of hot flashes, irritability, and reduced sleep. In addition, recent onset of vaginal dryness is causing dyspareunia that is not alleviated by lubricants. Her breast cancer was estrogen receptor (ER)/progesterone receptor (PR)–positive, and she received tamoxifen therapy for 5 years (now completed) following the...
initial diagnosis and management. How would you approach the management of this patient?

**Dr. Marjorie Jenkins:** I would first try to determine the severity of her hot flashes and how much her symptoms are affecting her quality of life. She may say that she is still having hot flashes, but how frequent are they? Do they cause nighttime awakening and subsequent fatigue?

**Dr. McKenzie:** The reason this patient presented was to ask for some form of relief because her symptoms were affecting her quality of life. Her dyspareunia was getting worse. She was trying various lubricants without success. At the same time, she expressed fear because her tumor was ER/PR-positive. Most cancer survivors have recurrence in the back of their mind even though they are in remission.

**Dr. Jenkins:** Was she asking specifically about HT or about help to relieve her symptoms?

**Dr. McKenzie:** She was asking for help for her symptoms.

**Dr. Jenkins:** I would consider low-dose vaginal estrogen to address her dyspareunia. I would also consider a serotonin-norepinephrine reuptake inhibitor, such as venlafaxine, to treat her hot flashes and irritability, along with lifestyle modifications, although the latter do not have evidence-based support. If these measures failed to offer relief, I would reconsider the risks and benefits of low-dose HT. I would call her oncologist for input if I planned to start vaginal estrogen, low-dose topical testosterone, or any type of hormonal treatment. I would make sure that the patient knew that her oncologist was working as part of the team responsible for her management.

**Dr. Thacker:** I concur. When I see hormonally sensitive breast cancer patients with vaginal symptoms, particularly when they are taking tamoxifen, I often talk to them about local estrogen before vaginal atrophy becomes severe. Once the atrophy becomes severe, local estrogen, even in low doses, may be absorbed systematically (increasing the risk of endometrial hyperplasia) until the vagina becomes re-estrogenized and stratified with healthy squamous epithelium. Once this restratification takes place, there are generally no systemic hormonal effects with low-dose local vaginal estrogen, but it is best to avoid severe atrophy in the first place. I like to start local estrogen early if I know that the oncologist wants to use an aromatase inhibitor in a breast cancer survivor. I prescribe the low-dose vaginal form frequently in my practice, and order transvaginal ultrasonography liberally if there is concern about the endometrium.

Additionally, I would offer this patient venlafaxine or, more specifically, desvenlafaxine, as the literature has shown that the latter agent is associated with an improvement in sleep. Currently, desvenlafaxine has been approved by the US Food and Drug Administration [FDA] solely to treat major depression; however, it has been studied in nondepressed women with hot flashes and is expected to be the first nonhormonal agent to receive FDA approval specifically to treat hot flashes.

**Dr. Gass:** This patient still has her uterus in place. Data show that estrogens have a first-pass uterine effect, and this gives me pause because estrogen levels could well be higher in the uterus than in the bloodstream. Because of those data, as well as the absence of long-term safety data, the use of estrogen in this patient would cause me concern.

With breast cancer patients in particular, I try everything else to treat vaginal dryness before adding estrogen. I believe that if a patient is having dyspareunia despite the use of adequate lubricants, something else is the problem. In many cases these women have not had intercourse for months because they have been undergoing treatment for breast cancer, and they can have hallmark pain syndromes or constriction of the vagina that may require treatments besides just estrogen. If all else failed, I would prescribe vaginal estrogen on a temporary basis. Women who stay sexually active after menopause can do perfectly fine without treatment, but those who have periods of abstinence and then try to resume sexual activity typically run into problems.

**Dr. Hodis:** Would you have concern about breast cancer recurrence with estrogen reinitiation, based on the literature?

**Dr. Gass:** I have seen recurrences out to 20 years after the initial cancer. If the cancer does recur, the woman will always have a nagging doubt that it could have been avoided if she had not used estrogen.

**Dr. Thacker:** We have many breast cancer survivors in our practice. It is an easier decision to give estrogen to women who have had bilateral mastectomy with...
reconstruction for a stage I breast cancer and have already had a hysterectomy or bilateral salpingo-oophorectomy. But we otherwise try to avoid it unless the patient has first tried everything else and is miserable from her vaginal symptoms.

Dr. Gass: When a patient is diagnosed with breast cancer, I gently encourage her to continue sexual activity through the course of treatment, explaining that she may be far better off later. It may avoid a lot of problems if we can proactively get that message across.

Dr. Jenkins: That is a great point, and there is evidence that increased sexual activity decreases vaginal atrophy and assists in maintaining vaginal elasticity and the ability of urogenital congestion with arousal. Although lubricants and moisturizers do work well, they may require repeated application, and inelasticity is still a problem for some patients. It is somewhat of a “use it or lose it” proposition.

Dr. Thacker: Recurrent urinary tract infections (UTIs) are a problem as well. Patients see urologists, undergo multiple endoscopies, and are treated with antibiotics, sometimes chronically, yet often they are not even offered local vaginal estrogen, which reduces recurrent UTIs. Local estrogen should be considered in any woman with vaginal atrophy and recurrent UTIs.

Case continued

Dr. McKenzie: To return to our case, this patient’s vagina was, in fact, severely constricted because she had not been sexually active for a while. Her BMI was initially greater than 25 kg/m², but she lost weight and became more symptomatic as she did so. She then stopped having sex because it was painful.

When she presented initially, she had a package of black cohosh with her and was willing to try it for her symptoms but was apprehensive after reading the disclaimers in the package. A 47-year-old who has already been diagnosed with ER-positive breast cancer is generally anxious about using any therapies that may be associated with an increased risk of breast cancer.

After examination of her vagina, her oncologist was consulted and suggested that her serum estradiol levels be measured; they were less than 20 pg/mL. We then agreed to a trial of estradiol vaginal tablets, vaginal dilators, and an increase in her sexual activity. She has been on vaginal estradiol for 2 years and is functioning very well. Her hot flashes improved spontaneously as her body adapted to her new weight.

I wonder how many more women would select HT if we told them about the 30% reduction in mortality despite the possibility of breast cancer diagnosis and DVT risks.

—Dr. Howard Hodis

BEYOND THE CASES: OTHER CHALLENGES IN MENOPAUSAL MANAGEMENT

HT discontinuation, dose reduction in real-world practice

Dr. Thacker: The first case we covered touched on both discontinuation of HT and HT dosage reduction. These are issues that come up often in clinical practice; what lessons does the panel have to share on these issues?

Dr. Gass: I find that there is a small subset of women who are highly symptomatic and are probably already going to be miserable whenever they try to go off HT. For some, if they are highly symptomatic at menopause, they tend to stay that way. They may try to go off, but a year later, they come back and say, “I am just too miserable.”

Dr. McKenzie: In my practice, I have noticed patients who end up staying on higher doses of HT for a long period because they do not tolerate weaning. If you take them down to 0.625 mg of estrogen, their hot flashes resume, so they seem to require 0.9 mg.

Dr. Thacker: I have a very small subset of those women too. I wonder if their metabolism is different; maybe 0.9 mg of conjugated equine estrogens is to them what 0.3 mg is to other women. As women get older, perhaps metabolic changes are one reason that many can reduce their hormone dosage. It is very challenging. I tell my students that it is much easier trying to determine how much thyroid hormone replacement to give a patient than how much estrogen.

When does transdermal estrogen make sense?

Dr. Sikon: I would be interested in the rest of the panel’s views on management of a woman in her early postmenopausal years who is symptomatic and has been on oral HT and is also a smoker. Would you switch her to transdermal estrogen or continue her oral HT and continue aggressive smoking cessation counseling?

Dr. Thacker: Many practitioners think that a smoker cannot take any type of HT because they equate it to oral/hormonal contraceptives, which increase the risk of heart attack in smokers over age 35, but hormonal contraceptives are different in that they involve a much higher dose of hormone. In my practice, the cases when I will offer transdermal estrogen are generally when a patient has gastrointestinal upset, known gallbladder disease, elevated triglycerides, or a prior
deep vein thrombosis (DVT), even though I will tell the patient that the HT-associated risks are still possible with transdermal therapies. Many women are inappropriately and inaccurately told that compounded transdermal therapies are “risk free.”

**Dr. McKenzie:** Transdermal estrogen is also an option for patients who are poor pill takers or are already taking too many pills. Many of my patients are on transdermal estrogen for the convenience that it offers. It is unfortunate that transdermal progesterone cream does not protect the endometrium in all patients; for women with a uterus, an oral progestogen needs to be prescribed. However, two transdermal patches containing progestogens have been shown to be efficacious in protecting the endometrium.

**How should a history of DVT affect decision-making?**

**Dr. McKenzie:** What do you do when a patient has a history of postoperative DVT and is already on HT? How many of the panel would discontinue the HT as opposed to continuing it?

**Dr. Hodis:** If it were a history of spontaneous DVT, I would feel uncomfortable continuing HT. A few years ago, a clinical trial was stopped early because women with a prior spontaneous DVT who were randomized to HT had a substantial increase in DVT incidence relative to those randomized to placebo.5 In the case of provoked or postoperative DVT, it may be a tougher call.

**Dr. Thacker:** I think that DVT is the greatest risk with HT, even though the media are more focused on breast cancer risk. The risk of breast cancer with estrogen alone is debatable, at least with oral conjugated estrogen, which was associated with a decreased risk in women who had undergone hysterectomy in the Women’s Health Initiative (WHI).6

When I see a woman with a history of DVT in my practice, I check her homocysteine levels and check for factor V Leiden and prothrombin gene mutation. If I find an inherited hypercoagulability disorder, I tell the patient that her risk of DVT with any type of hormone product is not just multiplicative, it is logarithmic. If the patient already requires lifelong anticoagulation, then I am a bit more comfortable with prescribing HT and I usually will try the transdermal route first; however, I always consider nonhormonal treatment alternatives first.

**Dr. Gass:** The WHI was supposed to have excluded women with a history of DVT, but a few such women were enrolled, and it was demonstrated that they were at higher risk of DVT recurrence if randomized to HT. The majority of DVT episodes in the WHI were spontaneous, not related to surgical procedures.

**Dr. Jenkins:** I have a patient who had been on low-dose HT for 30 years and underwent lumbar spine surgery. She had a somewhat prolonged recovery, so her lack of mobility and her age clearly increased her risk of DVT. So she was taken off HT and became miserable from the resulting hot flashes and sleep disturbance. We thoroughly discussed the risks and benefits of restarting HT, and because she was taking warfarin, we felt comfortable restarting the HT.

Women with spontaneous DVT are a different case, however, and I have an issue with restarting oral or transdermal HT in those cases. However, if we discuss the data with these patients and document the significant risks of HT in their cases, some may want to accept the increased risk in order to improve their quality of life, and that may be reasonable if they are truly fully informed.

**Dr. Thacker:** What about a woman who has been on oral contraceptives for several years and has not had a DVT? Is the safe use of oral/hormonal contraceptives something you take into account, Dr. Gass, in your decision whether to prescribe HT?

**Dr. Gass:** Yes, that can be reassuring. Twenty-seven percent of EPT participants and 49% of estrogen therapy (ET) participants in the WHI randomized trial had used hormones in the past, so it was as if they were already tested for an early risk of blood clots.7

**What role for SERMs (estrogen agonists/antagonists)?**

**Dr. Thacker:** I would like to discuss the use of estrogen agonists/estrogen antagonists, formerly known as selective estrogen receptor modulators (SERMs), such as raloxifene. Raloxifene now has an indication for breast cancer prevention as well as reduction of vertebral fractures. I don’t know if there is adequate recognition among practitioners that SERMs appear to be associated with the same risk of DVT that estrogen is, and a greater risk of fatal stroke.

**Dr. Jenkins:** I find the lack of hip fracture data with raloxifene concerning, because hip fracture carries
the highest 5-year mortality of any type of fracture. Raloxifene therefore is not a first-line agent for bone loss in my practice. But we also have to consider the patient’s risk of breast cancer and whether or not she has been on tamoxifen and now needs an agent to protect her against fracture. The question is whether we should consider starting these patients on raloxifene versus a bisphosphonate.

**Dr. Thacker:** Dr. Gass, do you think that raloxifene is safe for the endometrium? For years, we did not know the full effects of tamoxifen on the endometrium; it took experience with millions of patients to find out that tamoxifen increases the risk of endometrial cancer.

**Dr. Gass:** I do think that raloxifene is safer. I use it in my practice primarily for women younger than age 65 who are not yet at high risk for hip fracture but are still concerned about breast cancer. Although this concern diminishes as women age without having developed breast cancer, for younger women, who may see their friends getting breast cancer, it is a major concern. So if a patient is a good candidate for a bone loss agent and also has concern about breast cancer, raloxifene can be a good option, especially since we do not know what the implications are of taking bisphosphonates for 30 years. Questions about that are starting to be raised, so I think it is good to consider a sequential approach for some of these patients. A sequential approach might involve use of HT in a symptomatic menopausal woman, followed by use of raloxifene after the woman no longer has menopausal symptoms but is concerned about spine fracture protection and breast cancer risk reduction, followed by bisphosphonate use as she gets older and is at increased risk for stroke/VTE and for hip fracture.

**The challenge of educating younger doctors about HT**

**Dr. Thacker:** I think we need to find ways to translate the data on HT to younger generations of physicians, because the closer one is to graduating from medical school, the less likely he or she is to offer HT to an otherwise healthy, severely symptomatic woman younger than age 60.

**Dr. McKenzie:** Absolutely, and I think the real challenge is to reach younger physicians who go into private practice, who generally have the fewest opportunities to stay on top of the latest evidence. We must offer evidence-based education programs on this topic to physicians in the community to ensure that they are equipped to understand and explain the real risks and benefits of HT in order to individualize treatment decisions.

As a physician at a tertiary care center, I am surprised at the number of women referred to me who should have already been on HT for menopausal symptoms, but their physicians were unduly influenced by the initial WHI publication. They need to thoroughly evaluate their patients, assess their risks, assess any new medical problems, try to educate them, and then tailor therapy to improve their patients’ quality of life.

**Correcting misperceptions: WHI was not a treatment trial**

**Dr. Thacker:** I believe that many practitioners and especially students do not realize that the WHI was a trial designed to assess prevention of chronic diseases. It was not a menopausal treatment trial, and often its data are being misapplied to women who are different from the ones enrolled in the WHI, in that they are younger and more symptomatic.

**Dr. Gass:** It is correct that the WHI was not a treatment trial, but that was how HT was being used by some physicians and patients prior to the WHI. Physicians in this country were giving some 65-year-old women HT for osteoporosis and dementia. These practices needed to be supported with data, and that was the impetus behind the trial. Along the same lines, it is important how we present the risks to patients. If HT is being used as a therapy for a woman suffering from menopausal symptoms, she might be willing to accept more risk than if it is being used like a vitamin pill, to promote general health, in which case the risks should be virtually nil because the woman is healthy and without complaints.

**Dr. Thacker:** Yes, and that is why I think the earlier discussion of comparable risks of breast cancer, stroke, and VTE with aspirin, SERMs, fibric acid derivatives, and statins helps to put the risks of HT in perspective. It appears that physicians and patients tolerate very similar risks with commonly used nonhormonal medicines in women but do not tolerate any risks with HT, even in symptomatic women. In my opinion, this is a medical travesty. It is important to recognize that there are few absolutes in medicine that apply to all patients. The only universal recommendations I make to all patients are to wear seatbelts and not to smoke.

**Dr. Hodis:** What I find notable is that with HT we
see a reduction in mortality regardless of the risks that we have described. As the observational data show, if we start HT and continue it, there is a reduction in mortality of 30% or even greater, and the clinical trial data tend to support this benefit. So why do we shy away from HT? Because we are worried about a small increase in breast cancer diagnoses or a small increase in DVT? That is an issue I am grappling with.

**Dr. Thacker:** Similarly, how do you reconcile the observational data with aspirin? In the Nurses’ Health Study, the aspirin users had lower mortality, but in all of the randomized controlled trials in midlife women, we do not see a reduction in cardiovascular risk with aspirin, let alone a reduction in mortality. So, the people who self-select for treatment are obviously different from those enrolled in randomized trials. The randomized controlled trial may be our gold standard, but it is not necessarily the only evidence to consider.

**Dr. Hodis:** But there is a concordance between observational studies and randomized trials with respect to overall mortality and HT. The data from a meta-analysis of 30 randomized trials are consistent with the data from observational studies, even though they do identify risks. I wonder how many more women would select HT if we told them about the 30% reduction in mortality despite the possibility of breast cancer diagnosis and DVT risks.

**Dr. Gass:** Women will select according to their own agenda.

**Dr. Hodis:** Yes, in the end, it is all individualized.

**Dr. Gass:** Indeed, because women have specific concerns, such as breast cancer, fracture risk, or Alzheimer disease, and they base their personal decisions on these specific concerns. I educate them about the risks and benefits, and they pretty much decide for themselves. They know their priorities.

**Age and the risk-benefit assessment with HT**

**Dr. Thacker:** Does the panel have any comments on the recent position statement from the American Association of Clinical Endocrinologists concluding that the benefits of HT exceed the risks in symptomatic women younger than age 60?

**Dr. Hodis:** My only comment is to ask why it took them so long to come to that conclusion.

**Dr. Jenkins:** Also, too many people associate menopause only with hot flashes, without taking into account the increased risk of serious diseases that may occur at this time, such as osteoporosis and heart disease.

**Dr. Thacker:** That may be because menopause is a normal event. It can be a great time of life for many women; in fact, it is associated with lower rates of depression, unless there is a prolonged symptomatic perimenopause. Menopause is certainly not a disease, and NAMS has been very good at recognizing and promoting it as a normal phase of life. But to neglect treating a woman going through menopausal symptoms just because menopause is a normal life event would be akin to withholding assistance for women during childbirth, which is another natural event.

We fail from a medical perspective if we do not take care of symptomatic women, because they will then turn to people who are not physicians and who offer unregulated therapies. These people may deliver the right message—that menopausal women deserve to feel well and look good—but the way they tell women to treat menopausal symptoms is not science-based.
At one time, we were overtreating women and not individualizing therapy, but to me it is even more worrisome to withhold therapies unless women are so highly symptomatic that they consider ending their life. We are continuing to discover the risks and benefits of HT and how to further tailor it. We have many newer, lower-dose HT options, and we are expecting the first nonhormonal therapy for menopausal vasomotor symptoms, desvenlafaxine. We are fortunate to have bone agents and local vaginal therapies for women without vasomotor symptoms. With both hormonal and nonhormonal options, we must keep the risks and benefits of any therapy in perspective.

**CONCLUSIONS**

Dr. Thacker: This has been a great discussion, and although we do not all agree on every point, I would like to conclude by summarizing some key points on which I think we do all agree (see sidebar above). Menopause is a normal life event, but for some women who are symptomatic, and for a smaller percentage who will be symptomatic for the rest of their lives, HT is the gold standard, although it does not treat all symptoms and has some well-defined risks. We do have other options on the horizon for relief of vasomotor symptoms, for bone health, and for urogenital atrophy.

Following the data on the effects of HT on cardiovascular health will be particularly interesting. Although there is not support for using HT specifically for cardiovascular prevention, there are provocative data that in the symptomatic woman who has self-selected it, HT has cardiovascular benefit and reduces the risk of diabetes.

A woman on HT who has not had “early harm” does not need to arbitrarily discontinue therapy based on any time limit, as long as she is being periodically reevaluated and is offered individualized options.

**REFERENCES**


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### Risks and benefits of hormone therapy: The importance of timing

The benefits of HT (ET or EPT) vary based on the time of therapy initiation and the duration of use.

**Early menopausal years**

Starting HT in the early menopausal years is associated with relief of vasomotor symptoms, prevention of urogenital atrophy (and resulting dyspareunia), and reduction of the rapid bone loss that is prevalent in untreated women during the first 5 to 7 years following menopause. Use of HT during the early menopausal years may also be associated with a reduction in the risk of coronary heart disease.

The risks of HT during the early menopausal years include VTE, greater risk of increased breast density, and increased risk of gallbladder disease. The increased risk of breast cancer in women on short-term HT remains debatable.

In general, the benefits of HT outweight the risks in symptomatic menopausal women under the age of 60.

**Duration of use**

The duration of use is closely related to the risks and benefits of HT. The natural progression in most women is for vasomotor symptoms to decrease over time. With continued use of HT for 5 years or more, there are skeletal benefits, urogenital benefits, vasomotor symptom relief, and potential cardiovascular benefits if the patient was initially healthy when therapy was started. The risks with continued use of HT for more than 5 years remain VTE, stroke, and increased risk of breast cancer diagnosis.

**Ages 60 to 69**

For women 60 to 69 years old, the benefits of HT are vasomotor symptom relief (for those who remain symptomatic), prevention of urogenital atrophy, and prevention of bone loss and fracture. The risks are essentially the same as in younger women (VTE, stroke, and breast cancer), but these risks are increased compared with younger women, and HT dosage reduction should be considered.

**Ages 70 to 79**

Among women 70 to 79 years old, the skeletal and urogenital benefits of HT continue and the risks change slightly, to VTE, stroke, and coronary heart disease. The risks are increased particularly in women who have not been on systemic HT and who are starting HT at an advanced age, which is generally discouraged. Local vaginal estrogen should be considered in any woman with symptomatic urogenital atrophy.

**Clinical considerations**

The timing of HT initiation (relative to menopause) is a very important factor in the benefit-risk ratio. The patient’s age at menopause is also important. The benefits of HT outweigh the risks for most women in the early menopausal phase.

Recommendations for long-term therapy should consider the patient’s baseline risk factors, family history, duration of prior hormone use, the differential effects of ET and EPT, and the onset of new medical conditions.

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### ROUNDTABLE: CASE STUDIES AND CLINICAL CONSIDERATIONS

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