

## Chapter 1

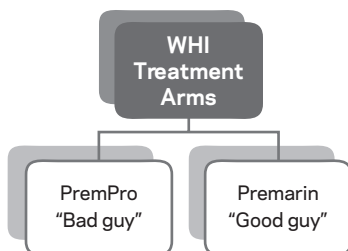
# Estrogen: Behind the Headlines



In the 35 years that I've been a doctor and women's health specialist, Estrogen has gone from hero to zero and back and forth again. How could this happen? How could the most frequently prescribed medication in America fall out of favor overnight? How could the same medication be so good and so bad, so loved and so hated, so beneficial and so harmful?

In this chapter we go behind the headlines and pull back the curtain to see how we got to this point and the circuitous path that took us there. Once the information becomes clear, it will be easy to understand how estrogen was blamed for problems it wasn't responsible for. The main characters in this story are Premarin (an estrogen only), which we'll call the "good guy," and Prempro (Premarin plus Provera), which we'll call the "bad guy." Prempro is a medication distinctly different from Premarin, though it contains Premarin, and as a result, Prempro has risks and benefits different from those of Premarin alone. I'll explain what these are later in the book and how to deal with them. I'll also show you how the estrogen window influences both of them.

The story begins at the end of a woman's reproductive years, when her reproductive hormones estrogen and progesterone transition from well-synchronized to unbalanced cycles that become progressively more unpredictable as she ages. During that window of time, estrogen levels fall, and the symptoms so typical of menopause begin to appear—hot flashes, vaginal dryness, embarrassing bladder symptoms, lower libido,

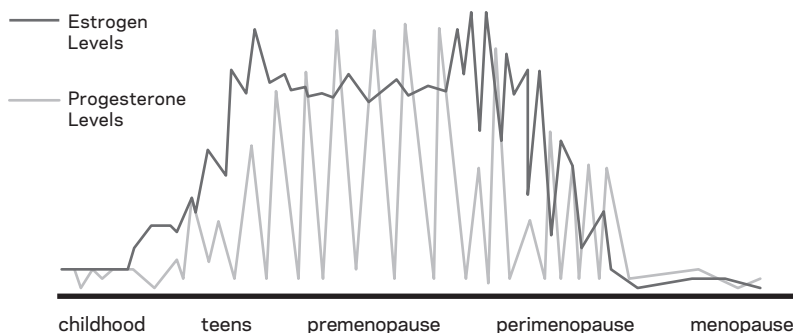


poor sleep, and more. It just makes sense that since all this happens as estrogen levels are falling, giving estrogen at that time would help decrease those symptoms—and it does.

So for several decades, doctors prescribed estrogen to women to relieve their perimenopausal and menopausal symptoms. But the plot thickens, because as I mentioned previously, there are two main characters, two hormones: estrogen and progesterone. I'll explain this in detail in the section on the history of estrogen.

If you look at a graph of the estrogen and progesterone levels during perimenopause, which is the time leading up to and just beyond menopause, it would look like a graph of the Dow Jones heading from a bull market into a recession. The zigzagging ups and downs trend downward and eventually remain low for the rest of a woman's life.

### Life Cycles of Ovarian Hormones



Perimenopause and early menopause are the times when most women start taking estrogen-containing medications, such as Premarin

and Prempro. Women traditionally *began* taking these medications within the first 10 years of entering menopause, because that's when their symptoms are usually worst.

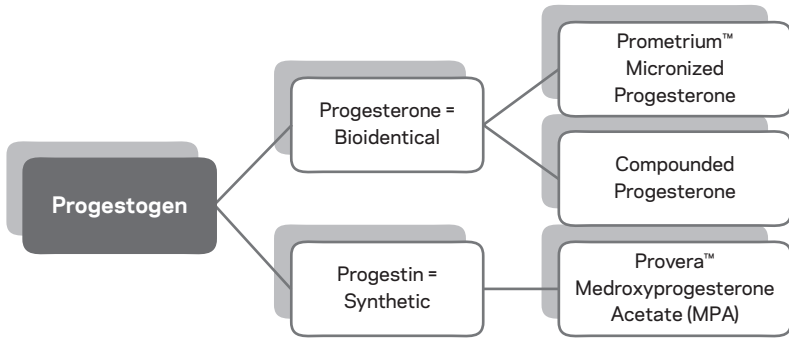
So why did the Women's Health Initiative (WHI) studies decide to give some women Premarin and others Prempro, and why did most of the women begin receiving medication between the ages of 60 and 79? It all depended on whether or not each woman still had her uterus. As you will see, this is a key point for understanding your estrogen window and how all the confusion got started.

Estrogen taken alone can lead to changes in the cells of the uterine lining over time; over a decade or more, these can turn into endometrial cancer. So Premarin, which is estrogen only, could not be safely used in women who had not had a hysterectomy. The good news is that if progesterone or a substance that acts in the body like progesterone (called a progestogen) is added, the risk of cancer of the uterine lining is virtually eliminated. So when the WHI studies were designed, women who had not had a hysterectomy were given Prempro, which contained Premarin and Provera. Women who had their uterus removed by hysterectomy were given Premarin (estrogen only).

Progesterone is the name of a hormone your body makes. Its name comes from "pro-gestation," because it prepares the uterine lining, which has been primed with estrogen, to receive and support a pregnancy. The use of Provera rather than progesterone in combination with estrogen in the WHI studies is what caused most of the problems and confusion about the risks and benefits of estrogen. As mentioned on page 1, Provera is the "bad guy."

At the beginning of the WHI studies, progesterone was not available as a pill, but Provera was, so that was prescribed. Prempro, which contained Premarin plus Provera, was a very popular pill at the time. Provera, like progesterone, is a *progestogen*, the term applied to any hormone that acts like progesterone in the body. Provera is the brand name for medroxyprogesterone acetate or MPA, a synthetic progestogen. Synthetic progestogens are called progestins. This incredibly confusing nomenclature is made even worse because when writing articles, many people use these terms interchangeably and incorrectly. A short biochemistry discussion will make a lot of things clearer when we discuss the WHI in more detail. The flow diagram on page 4 will help clarify

the information. While there are other synthetic progestins, I'll limit the discussion to Provera for now.



## The Women's Health Initiative

In 1991, the WHI under the aegis of the US National Institutes of Health (NIH) began a large-scale, long-term study that consisted of a set of clinical trials and an observational study, which together involved 161,808 “generally healthy” postmenopausal women aged 50 to 79 years. I put quotation marks around *generally healthy* because you'll see a little later that many of these women did have medical problems. The clinical trials were designed to test the effects of postmenopausal hormone therapy (HT), diet modification, and calcium and vitamin D supplements on heart disease, fractures, and breast and colorectal cancers.<sup>1</sup>

A lot of abbreviations are used to describe different hormone regimens, and as I mentioned earlier, they can have very different impacts. HT includes both Premarin and Prempro as well as any other estrogen alone or estrogen in combination with a progestogen. When estrogen is used alone, it is called estrogen therapy or ET; when estrogen is used together with a progestogen, it is called EPT. A major part of the confusion surrounding the WHI studies stems from the fact that the terms for these very different ways of giving estrogen are often used interchangeably. So whenever you read about risks and benefits of estrogen, be sure you understand what treatment the article is specifically referring to.

## Abbreviations in *The Estrogen Fix*

ET	Estrogen therapy	Estrogen alone: either oral, via skin, or vaginal—replaces ERT
EPT	Estrogen-progestogen therapy	Estrogen plus a hormone that acts like progesterone
HT	Hormone therapy	Estrogen alone or combined with a progestogen (progestin or progesterone)—replaces HRT
HRT	Hormone replacement therapy	See HT
ERT	Estrogen replacement therapy	Replaced by ET
MPA	Medroxyprogesterone acetate	A synthetic progestogen, also called a progestin
MHT	Menopausal hormone therapy	See HT

The first published WHI study compared a placebo with Prempro, which combines the conjugated estrogen Premarin with the synthetic progesterone medroxyprogesterone acetate (MPA sold as Provera), the most commonly prescribed progestin at the time of the study. Women in this study had a uterus and required the progestin to prevent cancer of the lining of the uterus. The second study compared a placebo to the estrogen Premarin in women who had their uterus removed (hysterectomy) and did not require a progestogen. The WHI study was supposed to continue for 15 years.

On July 9, 2002, after approximately 5.2 years, the WHI issued a news release saying that the Prempro study would be stopped effective immediately, because the data to date showed a definite link between Prempro and an increased risk of breast cancer or suffering a heart attack, blood clots, or stroke. The results made front-page, above-the-fold headlines in newspapers and were the opening stories on evening news programs. The *New York Times* called the findings “A Shock to the Medical System.” The *Washington Post* declared “A High Price for HT: No One Warned She Might Pay with Cancer.”

By 2002, 40 percent of postmenopausal women in the United States were using HT to relieve the debilitating symptoms of menopause—night sweats, hot flashes, heart palpitations, and moodiness. Overnight, sales of premarin dropped 73 percent as thousands of doctors stopped prescribing estrogen—all kinds of estrogen and any medicine containing estrogen. Millions of women, who felt they had been duped and used as

laboratory rats, instantly discontinued taking their estrogen-containing medicines. For those who insisted on continuing to use either Prempro or Premarin, many doctors required women to sign informed consents. Fear trumped reason, and front-page news affected doctors and their patients alike. Women and doctors had believed that estrogen was supposed to make women feel better without causing other medical issues; now doctors feared they had done their patients harm and patients believed they had been harmed.

It's difficult for many to remember or understand the panic that ensued when the WHI results were announced. To put it in historical perspective, just 10 months earlier America was attacked on September 11, 2001, and people were still feeling extremely vulnerable. When news of the canceled WHI study broke on July 9, 2002, many women felt as if they had been misled and were at risk of breast cancer, heart attack, and stroke. As many threw away their estrogen, anxiety levels skyrocketed.

I wish we could turn back the clock.

The 2002 WHI study contained a huge flaw that skewed the results and caused many women to forgo what we now know are the positive benefits of estrogen. I call these “estrogen myth-conceptions.”

After practicing medicine for so many years and seeing the positive results of prescribing estrogen, I was skeptical about the findings and

**SUSAN** was 52 and had gone through surgical menopause at age 49 after her uterus and ovaries were removed. When she came to see me, she was still struggling with hot flashes, and vaginal dryness had become a problem for her, so she decided she wanted to try taking estrogen. She had not taken it earlier because she was afraid of the risks, and now that she was asking for it, her doctor recommended she not take it because she felt that Susan's hot flashes were likely to stop soon. But Susan was just 3 years into menopause and early in her estrogen window, which made her a good candidate to take estrogen. We discussed the symptoms she was having and the options available to treat them, and addressed her fears about taking estrogen. After our discussion, she started on an estrogen patch and is now symptom-free well within her estrogen window.

was reluctant to change my opinion based on just one study. I continued to prescribe Premarin to those women who wanted to continue with it and tried to switch patients from Prempro to Premarin or other estrogens plus a bioidentical progesterone. Remember, the information about side effects of the 2002 WHI study had to do with Prempro, which contained Provera; it was not specifically a report on Premarin or estrogen alone—except that Premarin is an estrogen and Prempro does contain Premarin. Unfortunately, all estrogen-containing medications were lumped together and perceived as one and the same. As you'll find out, they aren't.

I began taking a detailed look at the 2002 WHI study and how the news-making conclusions were reached. When I did, I was stunned to discover that the controversy surrounding taking estrogen was based on flawed study design and misinterpreted data. I then began to uncover the flaws within the WHI study.

Up to this date, all the data had been observational, meaning there were no controls for comparisons. This new WHI study pulled the rug out from under all the previously published observations about estrogen. Not only had estrogen been perceived as safe and beneficial, but it was also used as a treatment for advanced breast cancer. This new idea that estrogen was bad and caused breast cancer, among other things, was a total reversal of the existing medical beliefs at that time.

I read and reread the study and its conclusions, spoke with leading doctors and researchers in the fields of women's health and menopause, and studied each new article that came out from the WHI and related sources. Remember that in 2004, just 2 years later, the estrogen-only arm of the WHI study did not show the same negative results; Premarin alone did not cause an increase in breast cancer or heart disease. So there were reasons to question the validity of the 2002 findings. A number of prominent doctors, including Wulf H. Utian, MD, who founded the North American Menopause Society, and Philip Sarrel, MD, of Yale University, didn't accept the study's findings as gospel, but evidence was necessary to prove that the results were wrong. The 2002 WHI study collected data in a quality way, but the big flaw was in the study design, and that caused incorrect interpretation of the information.

I owed it to my wife, Sharon, and my patients to learn everything about the topic, so they wouldn't have to choose between no treatment and treatment that they believed would alleviate their menopause symptoms but perhaps also increase their risk of death. Why should midlife women have to "tough it out" and suffer from their menopausal symptoms or live symptom-free and filled with fear and anxiety just because one study made claims unsubstantiated elsewhere?

My impression was that since participants in the 2004 study took estrogen only, and participants in both the 2002 and the 2004 studies received the same dosages of Premarin, the variable had to be Provera. Provera is known to narrow blood vessels and to undo the benefits of estrogen, which is part of the reason why I earlier referred to Provera as the bad guy. At that point I immediately stopped prescribing Provera, which was the progestogen combined with Premarin, and shifted my patients to bioidentical progesterone (see page 57).

I also noticed differences in the outcomes of the women in the two studies: The women in the 2004 Premarin-only study were also between the ages of 50 and 79, but when the study was stopped roughly 7 years after it began, those same women showed no increased risk of cardiovascular heart disease or heart attack and appeared to have *less* risk of breast cancer. For another 7 years there would not be enough numbers to prove that estrogen only lowered the risk of breast cancer.<sup>2</sup>

I saw a story beginning to take shape, but it would take me nearly a decade until further analysis of the same data and newer studies could prove that a woman's age and the number of years since she entered menopause play a major role when it comes to the risks and benefits of estrogen.

Prior to the first WHI study's findings in 2002, estrogen was thought to be a fountain of youth. Suddenly it was considered a risk factor for death and disease. As the study's flaws were being pointed out, the same doctors who once thought estrogen provided only positive benefits either didn't realize it or didn't want to go out on a limb and say they had it wrong yet again. I can appreciate how they felt, but not focusing on the facts would cause millions of women to continue not receiving estrogen, and I didn't want that to happen to them or to my wife.

I realized that the majority of women can safely take estrogen for effective relief of their menopausal symptoms starting at a certain time in their lives without having to worry about an increased risk of cancer,



heart disease, or other illnesses later. How? First, by revisiting the previous data, asking the right questions, and coming up with appropriate answers. Second, by publishing new studies that are better designed to ask the right question: When Premarin (estrogen only) or Prempro (estrogen plus progestogen) is given to a group of younger women and compared to women of similar age and medical histories who don't take these hormones, does estrogen offer benefits?

The answer is yes, particularly for the estrogen-only group. I can now confidently offer my patients estrogen and its many benefits. I can allay their fears by clarifying the misinformation published and publicized in 2002. Many of my patients are taking estrogen at the opportune time in life with great success. And there is plenty of evidence that you can too!

Unfortunately, today's media have been exceptionally silent about the subsequent reversal of thinking during the last several years as the results of better-designed estrogen studies have appeared. And to be fair, these new findings are also hard to believe because estrogen's dangers have become so ingrained in the minds of many. Again, here is the contrast: It's like a correction in the newspaper that is buried with other emendations and never receives the same attention as the error-filled story. This new information has largely gone unreported yet has remained hidden in clear view, which means that millions of women are suffering unnecessarily and jeopardizing their long-term health. Fortunately, organizations like the American College of Obstetricians and Gynecologists (ACOG), the North American Menopause Society (NAMS), the American Society for Reproductive Medicine (ASRM), and Advancing Health After Hysterectomy (Ahah) are also working to raise awareness of this issue.

Deciding whether or not to take estrogen is crucial for women today. In 1900 the average life span for a woman was 48 years, so not many women had to worry about menopause. Today is different. We live in a time when the average woman's life span is an astonishing 81 years and becoming longer every year. Questions about how to deal with menopause and the years beyond have become more frequent, more pressing, and much more relevant. A recent study showed that the number of women living to be 100 increased by 50 percent between 1990 and 2013,<sup>3</sup> but they have a number of health conditions. As more women (and men)

are living longer, enabling women to begin taking estrogen during their estrogen window will help them reach old age with fewer serious medical conditions and eliminate many menopause symptoms along the way. This is the basis of the estrogen fix.

## The History of Hormone Therapy

When the FDA approved the estrogen Premarin in 1942, for the first time, doctors immediately began to prescribe it to women to relieve their hot flashes and other symptoms of menopause. The estrogen revolution gained momentum in the 1950s, and in the 1960s estrogen's popularity continued to grow. To spread the word farther and faster, Wyeth-Ayerst Laboratories hired Brooklyn gynecologist Robert Wilson in 1966 to author *Feminine Forever* and extol the virtues of estrogen, even calling it a “fountain of youth” that would prevent the inevitable “living decay” of menopause.

By the late 1960s, Premarin was the most frequently prescribed drug in the United States.<sup>4</sup> Everyone wanted to take estrogen. For a while, it was even prescribed to men, but the results for men were harmful and sometimes fatal. And while everyone was seeking this “fountain of youth,” no one had yet discovered the optimum safe dosage required to do the job without unnecessary risk, what age to start taking it, or the length of time a woman should stay on the hormone. There was a growing understanding of the importance of taking a progestogen to protect the uterine lining—after long periods of estrogen alone, women would develop a precancerous tissue buildup called hyperplasia and a subset of those women would develop cancer of the uterine lining—but initially, the only commercially available progestogen was Provera. Provera had a number of worrisome side effects, including a possible increased risk of breast cancer, and it was not FDA approved for preventing uterine hyperplasia, so doctors weren't prescribing it along with Premarin. For these reasons, throughout much of this time, estrogen was given alone.

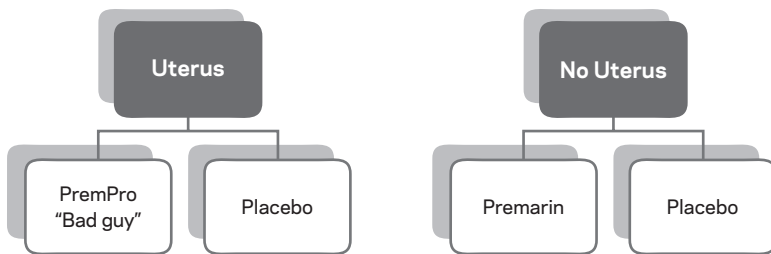
In 1975 and 1976 a series of three articles from three different centers were published in the *New England Journal of Medicine* that proved estrogen alone given to women with a uterus for long periods of time caused uterine cancer.<sup>5, 6, 7</sup> Public opinion immediately turned against estrogen, and its popularity tumbled.

In the 1980s evidence was growing that estrogen was helpful in preventing heart attacks in women. The belief that estrogen was cardioprotective was so strong that gynecologists and primary-care providers prescribed it not only to *treat* symptoms of menopause but also to *prevent* heart disease. Unfortunately, this information was based on observational studies, meaning they were not randomized with half of the women taking estrogen and the other half a placebo.

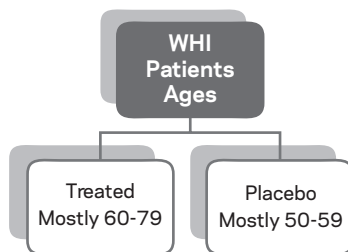
So to find out how estrogen might help prevent heart disease, a randomized study called the PEPI (Postmenopausal Estrogen/Progestin Interventions) Trial was established and included Premarin plus Provera.<sup>8</sup> A total of 875 women were studied for 3 years. When the results were published in 1995, Premarin plus Provera was found to have a positive effect on HDL or good cholesterol, and it protected the uterine lining cells from cancer. Following the PEPI Trial, the FDA approved Provera to prevent cancer of the uterine lining in postmenopausal women, and Provera became the most widely used progestogen for this purpose. Many unanswered questions remained, which is how Provera came to be tested in the WHI studies.

In the 1990s the WHI was created. Two different initial studies for two different groups of women with two different treatments were designed to last 15 years. Group one included 16,608 women who had a uterus, and they received either Prempro or a placebo. Group two included 10,739 women who did not have a uterus because of hysterectomy, and they received either Premarin or a placebo. These studies were the first multiyear, large-scale randomized clinical trials to determine the risks and benefits of these two types of medication on two groups of women. Premarin was still one of the most popular medications in the United States, as was Prempro, since Provera was now an FDA-approved medication to prevent cancer of the uterine lining.

In 2002 the first WHI study was abruptly shut down early at the 5.2 year mark after preliminary data indicated a small, measured increase in risk of breast cancer and cardiovascular heart disease among women who took Prempro. Since this was a prevention study, any increased health risk required that it immediately be discontinued. You can imagine that when the NIH shuts down a study and it becomes front-page news that suggests the medicine you are taking causes breast cancer and heart disease, you would panic if you were taking that medication. And panic causes lower objectivity. No one took the time to read the fine print.



The WHI studies had a “fatal” flaw. Instead of comparing apples with apples, they compared apples with oranges. They compared a placebo group of mostly younger women (mostly 50 to 59 years old) to a study group of mostly (75 percent) older women (mostly 60 to 79 years old). And to make matters worse, more than 60 percent of the women in the older group were lifelong smokers; many had some form of heart disease and were overweight. Many in the older group also had diabetes and high blood pressure. It’s no surprise that older women with more medical problems would have poorer outcomes—and they did.



Yet when the NIH released the 2002 WHI results, the risks were placed solely at the feet of the Prempro, which, as you’ll discover, did play a role; but the study did not consider preexisting risk factors or how much time had passed since each woman entered menopause. “Estrogen” was blamed entirely as the culprit. It was like comparing car death statistics between drunk or sleep-impaired drivers and those who were sober and rested. You don’t have to be a research scientist to know that this was poor science and poor analysis of the information. As mentioned, since this was a prevention study, any reported increase in risk meant the study had to be discontinued immediately.

The researchers running the study knew the women taking Prempro

were not comparable with the women in the control group because of the significant differences in age, but they didn't know how to overcome this hurdle. When the researchers first started recruiting subjects for the study in September 1993, so many menopausal women were already taking Premarin or Prempro, they had difficulty finding age-matched women for the control group who *weren't* taking it.

Instead they put together a group of women who were mostly aged 60 and over, all of whom were no longer taking Premarin or Prempro. But many of these women were heavy smokers and had poor heart health, diabetes, or high blood pressure. Yet amazingly, all that crucial health information and their age differences were overlooked and underreported when the WHI researchers wrote their conclusions about the safety and efficacy of Prempro. Many years later, these poorly analyzed, incorrectly interpreted data remain the basis of the misgivings and fears attached to estrogen. The patients who come to see me today as they enter menopause are still talking about those erroneous conclusions. I hear over and over again from these women that they feel they have no choice but to tough out their menopausal symptoms. It's as though taking any form of estrogen would be causing them early death. Almost every woman I see fears taking estrogen because of the outdated and incorrect WHI information. Once I explain the facts and reassure them, they become eager to discover their estrogen window.

## A Menopause Breakthrough

The confusion from the WHI study left me wondering what other studies, clinical trials, and information revealed about the positive versus negative effects of estrogen. I started reading all the estrogen information I could find to understand why estrogen continued to be the 800-pound gorilla in the room for menopause, women, and their doctors. I analyzed years of data, poring over major and minor studies and hundreds of peer-reviewed journal articles and papers presented at meetings and symposia. I interviewed fellow experienced doctors and top researchers, including Drs. Pauline Maki, Phil Sarrel, Wulf Utian, Isaac Schiff, Mary Jane Minkin, JoAnn V. Pinkerton, JoAnn E. Manson, James A. Simon, Sara Gottfried, Andrew Kaunitz, and others as editor of *The Hot Years-My Menopause Magazine*.

I did this because menopause is one of the most challenging periods in a woman's life. As an ob-gyn and menopause expert, I witness on an almost-daily basis how menopause symptoms affect the quality of my patients' lives and their performance in the workplace. Surely there had to be some evidence-based way that estrogen could be used to bring relief.

Each article, presentation, and interview contained a golden nugget of information that together created a pot of gold—something really valuable to help Sharon, my patients, and women everywhere. I came to realize there is such a thing I call the estrogen window, the time in a woman's life when she can most safely take estrogen and benefit from it in many ways.

Consider the hormone insulin for a diabetic patient. Taken at the right time, insulin regulates blood sugar, keeps diabetes under control, and wards off potentially devastating side effects. If insulin is given at the wrong time, a diabetic can go into diabetic shock. For estrogen, too, timing is very important. As a medication, it is not about being either good or bad. It's all about the timing. If taken at the right time, estrogen provides dramatic relief for the most troubling menopausal symptoms while at the same time providing a host of benefits, including:

- Extended protection from heart attacks and heart failure
- Reduced risk of Alzheimer's disease and other forms of cognitive decline
- Reduced risk of osteoporosis
- Beneficial cosmetic effects on the structure and resiliency of the skin
- Relief of sexual problems such as vaginal dryness and painful intercourse
- Relief from troubling and sometimes disabling hot flashes
- Improved quality of sleep
- Stabilized mood, particularly in women who have a known mental health diagnosis
- Lowered risk of type 2 diabetes
- Support for bladder tissue and lower risk of recurring urinary tract infections

Taken during a woman's estrogen window, estrogen accomplishes all these astonishing feats with minimal increased health risks. How long her estrogen window stays open depends on two things: which estrogen-containing medicine is used and which symptom or condition is being targeted, which I explain throughout *The Estrogen Fix*.

If the same woman takes the same drug after her estrogen window has closed, there may be an increased risk of serious side effects. Her odds for developing cardiovascular disease, blood clots, cancer, and cognitive decline become higher. But remember: It's not the estrogen that is bad; it's the Provera combined with the estrogen and *when* it is taken during a woman's life, or the timing, that are bad.

Too many women believe they have to struggle through this phase of life without assistance, and somehow if they do that and forgo estrogen, they will come out on the other side without any consequences. Others think that if they take estrogen and get almost immediate symptom relief, they will be diagnosed with breast cancer or heart disease a few years down the road. Nothing could be further from the truth. *The Estrogen Fix* will help you "figure it out" so you won't have to "tough it out."

It's ironic that the treatment women have avoided because they fear increased odds of developing a dreaded disease is in fact the very treatment that can offer greatly expanded protection *against* developing those same potentially deadly conditions *after* menopause. The key to using estrogen successfully is to take the right estrogen and to take it at the right time for at least 5 to 7 years following the onset of menopause.

It has taken decades to undo the damage done by one flawed study and change people's minds, even doctors', despite efforts from members of NAMS, ASRM, and ACOG. On June 3, 2015, NAMS<sup>9</sup> issued a statement and editorial on hormone therapy in women *after* age 65 that says:

- HT is the most effective treatment for symptoms of menopause.
- Vasomotor symptoms [hot flashes] may persist for more than a decade in many women and may continue in women after the age of 65, and these symptoms can disrupt sleep and adversely affect health and quality of life.
- Provided a woman has been advised of increased risks associated with continuing HT beyond age 60 and she has appropriate medical supervision, extending use of HT with the

lowest effective dose is acceptable under some circumstances in women older than 65.

- Use of HT should be individualized and not discontinued based solely on a woman's age.

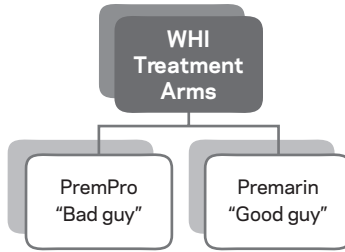
On October 6, 2016, at the NAMS Annual Scientific Meeting, Executive Director JoAnn V. Pinkerton, MD, revealed their latest position statement about HT, which represents a consensus of over 20 international experts.<sup>10</sup>

The bottom line: Overall, HT has clear benefits for the treatment of hot flashes and bone loss prevention. These benefits are most favorable among women aged younger than 60 years who are within 10 years of menopause onset and have no medical reasons they can't take HT. Women older than age 60 who begin HT beyond 10 years of menopause onset appear to have a less favorable benefit-risk ratio because of elevated risks of coronary heart disease, stroke, venous thromboembolism, and dementia—i.e., it's all about the estrogen window.

The science is clear: Based on clinical studies that have appeared in multiple peer-reviewed medical journals, estrogen *can* be taken safely if used in the right way at the right time for the right length of time.

If you're like my patients, you probably have a lot of questions: Is estrogen really as safe as you say? Do I take pills, use a cream, or apply a patch? What's the right dosage for me? When should I start? How do I know when to stop? Which estrogen should I take? Which progestogen should I take? All your questions will be answered in *The Estrogen Fix*, so you'll be prepared to have an informed conversation with your physician or health-care provider.



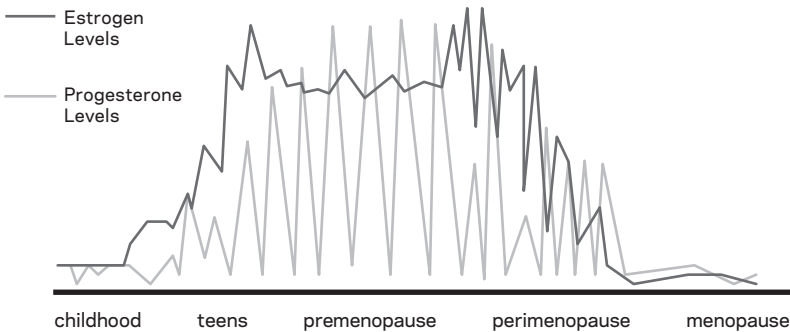


poor sleep, and more. It just makes sense that since all this happens as estrogen levels are falling, giving estrogen at that time would help decrease those symptoms—and it does.

So for several decades, doctors prescribed estrogen to women to relieve their perimenopausal and menopausal symptoms. But the plot thickens, because as I mentioned previously, there are two main characters, two hormones: estrogen and progesterone. I'll explain this in detail in the section on the history of estrogen.

If you look at a graph of the estrogen and progesterone levels during perimenopause, which is the time leading up to and just beyond menopause, it would look like a graph of the Dow Jones heading from a bull market into a recession. The zigzagging ups and downs trend downward and eventually remain low for the rest of a woman's life.

### Life Cycles of Ovarian Hormones



Perimenopause and early menopause are the times when most women start taking estrogen-containing medications, such as Premarin

and Prempro. Women traditionally *began* taking these medications within the first 10 years of entering menopause, because that's when their symptoms are usually worst.

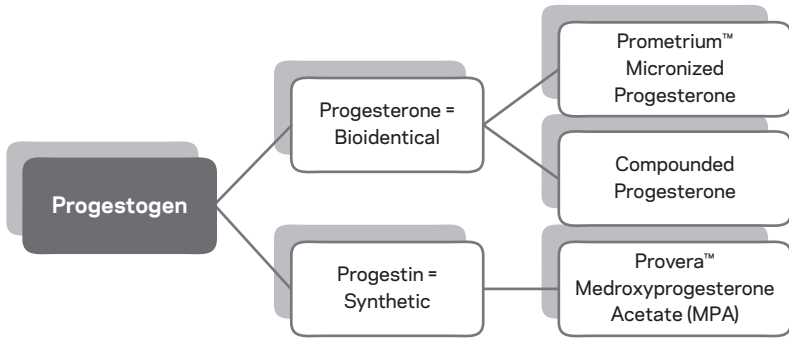
So why did the Women's Health Initiative (WHI) studies decide to give some women Premarin and others Prempro, and why did most of the women begin receiving medication between the ages of 60 and 79? It all depended on whether or not each woman still had her uterus. As you will see, this is a key point for understanding your estrogen window and how all the confusion got started.

Estrogen taken alone can lead to changes in the cells of the uterine lining over time; over a decade or more, these can turn into endometrial cancer. So Premarin, which is estrogen only, could not be safely used in women who had not had a hysterectomy. The good news is that if progesterone or a substance that acts in the body like progesterone (called a progestogen) is added, the risk of cancer of the uterine lining is virtually eliminated. So when the WHI studies were designed, women who had not had a hysterectomy were given Prempro, which contained Premarin and Provera. Women who had their uterus removed by hysterectomy were given Premarin (estrogen only).

Progesterone is the name of a hormone your body makes. Its name comes from "pro-gestation," because it prepares the uterine lining, which has been primed with estrogen, to receive and support a pregnancy. The use of Provera rather than progesterone in combination with estrogen in the WHI studies is what caused most of the problems and confusion about the risks and benefits of estrogen. As mentioned on page 1, Provera is the "bad guy."

At the beginning of the WHI studies, progesterone was not available as a pill, but Provera was, so that was prescribed. Prempro, which contained Premarin plus Provera, was a very popular pill at the time. Provera, like progesterone, is a *progestogen*, the term applied to any hormone that acts like progesterone in the body. Provera is the brand name for medroxyprogesterone acetate or MPA, a synthetic progestogen. Synthetic progestogens are called progestins. This incredibly confusing nomenclature is made even worse because when writing articles, many people use these terms interchangeably and incorrectly. A short biochemistry discussion will make a lot of things clearer when we discuss the WHI in more detail. The flow diagram on page 4 will help clarify

the information. While there are other synthetic progestins, I'll limit the discussion to Provera for now.



## The Women’s Health Initiative

In 1991, the WHI under the aegis of the US National Institutes of Health (NIH) began a large-scale, long-term study that consisted of a set of clinical trials and an observational study, which together involved 161,808 “generally healthy” postmenopausal women aged 50 to 79 years. I put quotation marks around *generally healthy* because you’ll see a little later that many of these women did have medical problems. The clinical trials were designed to test the effects of postmenopausal hormone therapy (HT), diet modification, and calcium and vitamin D supplements on heart disease, fractures, and breast and colorectal cancers.<sup>1</sup>

A lot of abbreviations are used to describe different hormone regimens, and as I mentioned earlier, they can have very different impacts. HT includes both Premarin and Prempro as well as any other estrogen alone or estrogen in combination with a progestogen. When estrogen is used alone, it is called estrogen therapy or ET; when estrogen is used together with a progestogen, it is called EPT. A major part of the confusion surrounding the WHI studies stems from the fact that the terms for these very different ways of giving estrogen are often used interchangeably. So whenever you read about risks and benefits of estrogen, be sure you understand what treatment the article is specifically referring to.

## Abbreviations in *The Estrogen Fix*

ET	Estrogen therapy	Estrogen alone: either oral, via skin, or vaginal—replaces ERT
EPT	Estrogen-progestogen therapy	Estrogen plus a hormone that acts like progesterone
HT	Hormone therapy	Estrogen alone or combined with a progestogen (progestin or progesterone)—replaces HRT
HRT	Hormone replacement therapy	See HT
ERT	Estrogen replacement therapy	Replaced by ET
MPA	Medroxyprogesterone acetate	A synthetic progestogen, also called a progestin
MHT	Menopausal hormone therapy	See HT

The first published WHI study compared a placebo with Prempro, which combines the conjugated estrogen Premarin with the synthetic progesterone medroxyprogesterone acetate (MPA sold as Provera), the most commonly prescribed progestin at the time of the study. Women in this study had a uterus and required the progestin to prevent cancer of the lining of the uterus. The second study compared a placebo to the estrogen Premarin in women who had their uterus removed (hysterectomy) and did not require a progestogen. The WHI study was supposed to continue for 15 years.

On July 9, 2002, after approximately 5.2 years, the WHI issued a news release saying that the Prempro study would be stopped effective immediately, because the data to date showed a definite link between Prempro and an increased risk of breast cancer or suffering a heart attack, blood clots, or stroke. The results made front-page, above-the-fold headlines in newspapers and were the opening stories on evening news programs. The *New York Times* called the findings “A Shock to the Medical System.” The *Washington Post* declared “A High Price for HT: No One Warned She Might Pay with Cancer.”

By 2002, 40 percent of postmenopausal women in the United States were using HT to relieve the debilitating symptoms of menopause—night sweats, hot flashes, heart palpitations, and moodiness. Overnight, sales of premarin dropped 73 percent as thousands of doctors stopped prescribing estrogen—all kinds of estrogen and any medicine containing estrogen. Millions of women, who felt they had been duped and used as

laboratory rats, instantly discontinued taking their estrogen-containing medicines. For those who insisted on continuing to use either Prempro or Premarin, many doctors required women to sign informed consents. Fear trumped reason, and front-page news affected doctors and their patients alike. Women and doctors had believed that estrogen was supposed to make women feel better without causing other medical issues; now doctors feared they had done their patients harm and patients believed they had been harmed.

It's difficult for many to remember or understand the panic that ensued when the WHI results were announced. To put it in historical perspective, just 10 months earlier America was attacked on September 11, 2001, and people were still feeling extremely vulnerable. When news of the canceled WHI study broke on July 9, 2002, many women felt as if they had been misled and were at risk of breast cancer, heart attack, and stroke. As many threw away their estrogen, anxiety levels skyrocketed.

I wish we could turn back the clock.

The 2002 WHI study contained a huge flaw that skewed the results and caused many women to forgo what we now know are the positive benefits of estrogen. I call these “estrogen myth-conceptions.”

After practicing medicine for so many years and seeing the positive results of prescribing estrogen, I was skeptical about the findings and

**SUSAN** was 52 and had gone through surgical menopause at age 49 after her uterus and ovaries were removed. When she came to see me, she was still struggling with hot flashes, and vaginal dryness had become a problem for her, so she decided she wanted to try taking estrogen. She had not taken it earlier because she was afraid of the risks, and now that she was asking for it, her doctor recommended she not take it because she felt that Susan's hot flashes were likely to stop soon. But Susan was just 3 years into menopause and early in her estrogen window, which made her a good candidate to take estrogen. We discussed the symptoms she was having and the options available to treat them, and addressed her fears about taking estrogen. After our discussion, she started on an estrogen patch and is now symptom-free well within her estrogen window.

was reluctant to change my opinion based on just one study. I continued to prescribe Premarin to those women who wanted to continue with it and tried to switch patients from Prempro to Premarin or other estrogens plus a bioidentical progesterone. Remember, the information about side effects of the 2002 WHI study had to do with Prempro, which contained Provera; it was not specifically a report on Premarin or estrogen alone—except that Premarin is an estrogen and Prempro does contain Premarin. Unfortunately, all estrogen-containing medications were lumped together and perceived as one and the same. As you'll find out, they aren't.

I began taking a detailed look at the 2002 WHI study and how the news-making conclusions were reached. When I did, I was stunned to discover that the controversy surrounding taking estrogen was based on flawed study design and misinterpreted data. I then began to uncover the flaws within the WHI study.

Up to this date, all the data had been observational, meaning there were no controls for comparisons. This new WHI study pulled the rug out from under all the previously published observations about estrogen. Not only had estrogen been perceived as safe and beneficial, but it was also used as a treatment for advanced breast cancer. This new idea that estrogen was bad and caused breast cancer, among other things, was a total reversal of the existing medical beliefs at that time.

I read and reread the study and its conclusions, spoke with leading doctors and researchers in the fields of women's health and menopause, and studied each new article that came out from the WHI and related sources. Remember that in 2004, just 2 years later, the estrogen-only arm of the WHI study did not show the same negative results; Premarin alone did not cause an increase in breast cancer or heart disease. So there were reasons to question the validity of the 2002 findings. A number of prominent doctors, including Wulf H. Utian, MD, who founded the North American Menopause Society, and Philip Sarrel, MD, of Yale University, didn't accept the study's findings as gospel, but evidence was necessary to prove that the results were wrong. The 2002 WHI study collected data in a quality way, but the big flaw was in the study design, and that caused incorrect interpretation of the information.

I owed it to my wife, Sharon, and my patients to learn everything about the topic, so they wouldn't have to choose between no treatment and treatment that they believed would alleviate their menopause symptoms but perhaps also increase their risk of death. Why should midlife women have to "tough it out" and suffer from their menopausal symptoms or live symptom-free and filled with fear and anxiety just because one study made claims unsubstantiated elsewhere?

My impression was that since participants in the 2004 study took estrogen only, and participants in both the 2002 and the 2004 studies received the same dosages of Premarin, the variable had to be Provera. Provera is known to narrow blood vessels and to undo the benefits of estrogen, which is part of the reason why I earlier referred to Provera as the bad guy. At that point I immediately stopped prescribing Provera, which was the progestogen combined with Premarin, and shifted my patients to bioidentical progesterone (see page 57).

I also noticed differences in the outcomes of the women in the two studies: The women in the 2004 Premarin-only study were also between the ages of 50 and 79, but when the study was stopped roughly 7 years after it began, those same women showed no increased risk of cardiovascular heart disease or heart attack and appeared to have *less* risk of breast cancer. For another 7 years there would not be enough numbers to prove that estrogen only lowered the risk of breast cancer.<sup>2</sup>

I saw a story beginning to take shape, but it would take me nearly a decade until further analysis of the same data and newer studies could prove that a woman's age and the number of years since she entered menopause play a major role when it comes to the risks and benefits of estrogen.

Prior to the first WHI study's findings in 2002, estrogen was thought to be a fountain of youth. Suddenly it was considered a risk factor for death and disease. As the study's flaws were being pointed out, the same doctors who once thought estrogen provided only positive benefits either didn't realize it or didn't want to go out on a limb and say they had it wrong yet again. I can appreciate how they felt, but not focusing on the facts would cause millions of women to continue not receiving estrogen, and I didn't want that to happen to them or to my wife.

I realized that the majority of women can safely take estrogen for effective relief of their menopausal symptoms starting at a certain time in their lives without having to worry about an increased risk of cancer,

heart disease, or other illnesses later. How? First, by revisiting the previous data, asking the right questions, and coming up with appropriate answers. Second, by publishing new studies that are better designed to ask the right question: When Premarin (estrogen only) or Prempro (estrogen plus progestogen) is given to a group of younger women and compared to women of similar age and medical histories who don't take these hormones, does estrogen offer benefits?

The answer is yes, particularly for the estrogen-only group. I can now confidently offer my patients estrogen and its many benefits. I can allay their fears by clarifying the misinformation published and publicized in 2002. Many of my patients are taking estrogen at the opportune time in life with great success. And there is plenty of evidence that you can too!

Unfortunately, today's media have been exceptionally silent about the subsequent reversal of thinking during the last several years as the results of better-designed estrogen studies have appeared. And to be fair, these new findings are also hard to believe because estrogen's dangers have become so ingrained in the minds of many. Again, here is the contrast: It's like a correction in the newspaper that is buried with other emendations and never receives the same attention as the error-filled story. This new information has largely gone unreported yet has remained hidden in clear view, which means that millions of women are suffering unnecessarily and jeopardizing their long-term health. Fortunately, organizations like the American College of Obstetricians and Gynecologists (ACOG), the North American Menopause Society (NAMS), the American Society for Reproductive Medicine (ASRM), and Advancing Health After Hysterectomy (Ahah) are also working to raise awareness of this issue.

Deciding whether or not to take estrogen is crucial for women today. In 1900 the average life span for a woman was 48 years, so not many women had to worry about menopause. Today is different. We live in a time when the average woman's life span is an astonishing 81 years and becoming longer every year. Questions about how to deal with menopause and the years beyond have become more frequent, more pressing, and much more relevant. A recent study showed that the number of women living to be 100 increased by 50 percent between 1990 and 2013,<sup>3</sup> but they have a number of health conditions. As more women (and men)



are living longer, enabling women to begin taking estrogen during their estrogen window will help them reach old age with fewer serious medical conditions and eliminate many menopause symptoms along the way. This is the basis of the estrogen fix.

## The History of Hormone Therapy

When the FDA approved the estrogen Premarin in 1942, for the first time, doctors immediately began to prescribe it to women to relieve their hot flashes and other symptoms of menopause. The estrogen revolution gained momentum in the 1950s, and in the 1960s estrogen's popularity continued to grow. To spread the word farther and faster, Wyeth-Ayerst Laboratories hired Brooklyn gynecologist Robert Wilson in 1966 to author *Feminine Forever* and extol the virtues of estrogen, even calling it a “fountain of youth” that would prevent the inevitable “living decay” of menopause.

By the late 1960s, Premarin was the most frequently prescribed drug in the United States.<sup>4</sup> Everyone wanted to take estrogen. For a while, it was even prescribed to men, but the results for men were harmful and sometimes fatal. And while everyone was seeking this “fountain of youth,” no one had yet discovered the optimum safe dosage required to do the job without unnecessary risk, what age to start taking it, or the length of time a woman should stay on the hormone. There was a growing understanding of the importance of taking a progestogen to protect the uterine lining—after long periods of estrogen alone, women would develop a precancerous tissue buildup called hyperplasia and a subset of those women would develop cancer of the uterine lining—but initially, the only commercially available progestogen was Provera. Provera had a number of worrisome side effects, including a possible increased risk of breast cancer, and it was not FDA approved for preventing uterine hyperplasia, so doctors weren't prescribing it along with Premarin. For these reasons, throughout much of this time, estrogen was given alone.

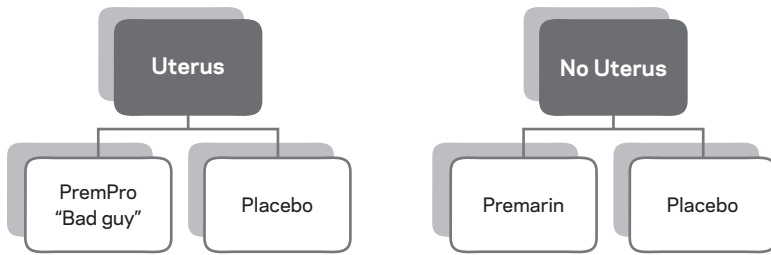
In 1975 and 1976 a series of three articles from three different centers were published in the *New England Journal of Medicine* that proved estrogen alone given to women with a uterus for long periods of time caused uterine cancer.<sup>5, 6, 7</sup> Public opinion immediately turned against estrogen, and its popularity tumbled.

In the 1980s evidence was growing that estrogen was helpful in preventing heart attacks in women. The belief that estrogen was cardioprotective was so strong that gynecologists and primary-care providers prescribed it not only to *treat* symptoms of menopause but also to *prevent* heart disease. Unfortunately, this information was based on observational studies, meaning they were not randomized with half of the women taking estrogen and the other half a placebo.

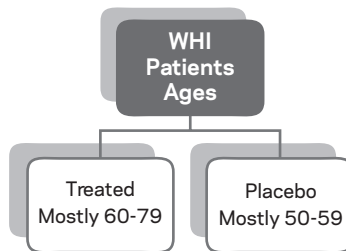
So to find out how estrogen might help prevent heart disease, a randomized study called the PEPI (Postmenopausal Estrogen/Progestin Interventions) Trial was established and included Premarin plus Provera.<sup>8</sup> A total of 875 women were studied for 3 years. When the results were published in 1995, Premarin plus Provera was found to have a positive effect on HDL or good cholesterol, and it protected the uterine lining cells from cancer. Following the PEPI Trial, the FDA approved Provera to prevent cancer of the uterine lining in postmenopausal women, and Provera became the most widely used progestogen for this purpose. Many unanswered questions remained, which is how Provera came to be tested in the WHI studies.

In the 1990s the WHI was created. Two different initial studies for two different groups of women with two different treatments were designed to last 15 years. Group one included 16,608 women who had a uterus, and they received either Prempro or a placebo. Group two included 10,739 women who did not have a uterus because of hysterectomy, and they received either Premarin or a placebo. These studies were the first multiyear, large-scale randomized clinical trials to determine the risks and benefits of these two types of medication on two groups of women. Premarin was still one of the most popular medications in the United States, as was Prempro, since Provera was now an FDA-approved medication to prevent cancer of the uterine lining.

In 2002 the first WHI study was abruptly shut down early at the 5.2 year mark after preliminary data indicated a small, measured increase in risk of breast cancer and cardiovascular heart disease among women who took Prempro. Since this was a prevention study, any increased health risk required that it immediately be discontinued. You can imagine that when the NIH shuts down a study and it becomes front-page news that suggests the medicine you are taking causes breast cancer and heart disease, you would panic if you were taking that medication. And panic causes lower objectivity. No one took the time to read the fine print.



The WHI studies had a “fatal” flaw. Instead of comparing apples with apples, they compared apples with oranges. They compared a placebo group of mostly younger women (mostly 50 to 59 years old) to a study group of mostly (75 percent) older women (mostly 60 to 79 years old). And to make matters worse, more than 60 percent of the women in the older group were lifelong smokers; many had some form of heart disease and were overweight. Many in the older group also had diabetes and high blood pressure. It’s no surprise that older women with more medical problems would have poorer outcomes—and they did.



Yet when the NIH released the 2002 WHI results, the risks were placed solely at the feet of the Prempro, which, as you’ll discover, did play a role; but the study did not consider preexisting risk factors or how much time had passed since each woman entered menopause. “Estrogen” was blamed entirely as the culprit. It was like comparing car death statistics between drunk or sleep-impaired drivers and those who were sober and rested. You don’t have to be a research scientist to know that this was poor science and poor analysis of the information. As mentioned, since this was a prevention study, any reported increase in risk meant the study had to be discontinued immediately.

The researchers running the study knew the women taking Prempro

were not comparable with the women in the control group because of the significant differences in age, but they didn't know how to overcome this hurdle. When the researchers first started recruiting subjects for the study in September 1993, so many menopausal women were already taking Premarin or Prempro, they had difficulty finding age-matched women for the control group who *weren't* taking it.

Instead they put together a group of women who were mostly aged 60 and over, all of whom were no longer taking Premarin or Prempro. But many of these women were heavy smokers and had poor heart health, diabetes, or high blood pressure. Yet amazingly, all that crucial health information and their age differences were overlooked and underreported when the WHI researchers wrote their conclusions about the safety and efficacy of Prempro. Many years later, these poorly analyzed, incorrectly interpreted data remain the basis of the misgivings and fears attached to estrogen. The patients who come to see me today as they enter menopause are still talking about those erroneous conclusions. I hear over and over again from these women that they feel they have no choice but to tough out their menopausal symptoms. It's as though taking any form of estrogen would be causing them early death. Almost every woman I see fears taking estrogen because of the outdated and incorrect WHI information. Once I explain the facts and reassure them, they become eager to discover their estrogen window.

## A Menopause Breakthrough

The confusion from the WHI study left me wondering what other studies, clinical trials, and information revealed about the positive versus negative effects of estrogen. I started reading all the estrogen information I could find to understand why estrogen continued to be the 800-pound gorilla in the room for menopause, women, and their doctors. I analyzed years of data, poring over major and minor studies and hundreds of peer-reviewed journal articles and papers presented at meetings and symposia. I interviewed fellow experienced doctors and top researchers, including Drs. Pauline Maki, Phil Sarrel, Wulf Utian, Isaac Schiff, Mary Jane Minkin, JoAnn V. Pinkerton, JoAnn E. Manson, James A. Simon, Sara Gottfried, Andrew Kaunitz, and others as editor of *The Hot Years-My Menopause Magazine*.

I did this because menopause is one of the most challenging periods in a woman's life. As an ob-gyn and menopause expert, I witness on an almost-daily basis how menopause symptoms affect the quality of my patients' lives and their performance in the workplace. Surely there had to be some evidence-based way that estrogen could be used to bring relief.

Each article, presentation, and interview contained a golden nugget of information that together created a pot of gold—something really valuable to help Sharon, my patients, and women everywhere. I came to realize there is such a thing I call the estrogen window, the time in a woman's life when she can most safely take estrogen and benefit from it in many ways.

Consider the hormone insulin for a diabetic patient. Taken at the right time, insulin regulates blood sugar, keeps diabetes under control, and wards off potentially devastating side effects. If insulin is given at the wrong time, a diabetic can go into diabetic shock. For estrogen, too, timing is very important. As a medication, it is not about being either good or bad. It's all about the timing. If taken at the right time, estrogen provides dramatic relief for the most troubling menopausal symptoms while at the same time providing a host of benefits, including:

- Extended protection from heart attacks and heart failure
- Reduced risk of Alzheimer's disease and other forms of cognitive decline
- Reduced risk of osteoporosis
- Beneficial cosmetic effects on the structure and resiliency of the skin
- Relief of sexual problems such as vaginal dryness and painful intercourse
- Relief from troubling and sometimes disabling hot flashes
- Improved quality of sleep
- Stabilized mood, particularly in women who have a known mental health diagnosis
- Lowered risk of type 2 diabetes
- Support for bladder tissue and lower risk of recurring urinary tract infections

Taken during a woman's estrogen window, estrogen accomplishes all these astonishing feats with minimal increased health risks. How long her estrogen window stays open depends on two things: which estrogen-containing medicine is used and which symptom or condition is being targeted, which I explain throughout *The Estrogen Fix*.

If the same woman takes the same drug after her estrogen window has closed, there may be an increased risk of serious side effects. Her odds for developing cardiovascular disease, blood clots, cancer, and cognitive decline become higher. But remember: It's not the estrogen that is bad; it's the Provera combined with the estrogen and *when* it is taken during a woman's life, or the timing, that are bad.

Too many women believe they have to struggle through this phase of life without assistance, and somehow if they do that and forgo estrogen, they will come out on the other side without any consequences. Others think that if they take estrogen and get almost immediate symptom relief, they will be diagnosed with breast cancer or heart disease a few years down the road. Nothing could be further from the truth. *The Estrogen Fix* will help you "figure it out" so you won't have to "tough it out."

It's ironic that the treatment women have avoided because they fear increased odds of developing a dreaded disease is in fact the very treatment that can offer greatly expanded protection *against* developing those same potentially deadly conditions *after* menopause. The key to using estrogen successfully is to take the right estrogen and to take it at the right time for at least 5 to 7 years following the onset of menopause.

It has taken decades to undo the damage done by one flawed study and change people's minds, even doctors', despite efforts from members of NAMS, ASRM, and ACOG. On June 3, 2015, NAMS<sup>9</sup> issued a statement and editorial on hormone therapy in women *after* age 65 that says:

- HT is the most effective treatment for symptoms of menopause.
- Vasomotor symptoms [hot flashes] may persist for more than a decade in many women and may continue in women after the age of 65, and these symptoms can disrupt sleep and adversely affect health and quality of life.
- Provided a woman has been advised of increased risks associated with continuing HT beyond age 60 and she has appropriate medical supervision, extending use of HT with the

lowest effective dose is acceptable under some circumstances in women older than 65.

- Use of HT should be individualized and not discontinued based solely on a woman's age.

On October 6, 2016, at the NAMS Annual Scientific Meeting, Executive Director JoAnn V. Pinkerton, MD, revealed their latest position statement about HT, which represents a consensus of over 20 international experts.<sup>10</sup>

The bottom line: Overall, HT has clear benefits for the treatment of hot flashes and bone loss prevention. These benefits are most favorable among women aged younger than 60 years who are within 10 years of menopause onset and have no medical reasons they can't take HT. Women older than age 60 who begin HT beyond 10 years of menopause onset appear to have a less favorable benefit-risk ratio because of elevated risks of coronary heart disease, stroke, venous thromboembolism, and dementia—i.e., it's all about the estrogen window.

The science is clear: Based on clinical studies that have appeared in multiple peer-reviewed medical journals, estrogen *can* be taken safely if used in the right way at the right time for the right length of time.

If you're like my patients, you probably have a lot of questions: Is estrogen really as safe as you say? Do I take pills, use a cream, or apply a patch? What's the right dosage for me? When should I start? How do I know when to stop? Which estrogen should I take? Which progestogen should I take? All your questions will be answered in *The Estrogen Fix*, so you'll be prepared to have an informed conversation with your physician or health-care provider.