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REPORT

What You Don't Know About Estrogen

There are many misconceptions about what estrogen really is and how it works in the body. This widespread confusion exists in the minds of the lay public as well as the medical community. The result is poor choices being made about what women should be doing to maintain youthful hormone balance while also protecting against cancer.

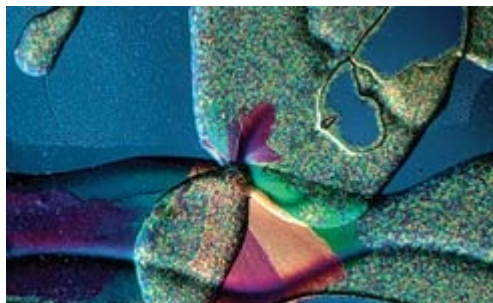
This article uncovers the basic facts about estrogen that are so often overlooked by doctors today. It then reveals dietary modifications that women should consider if they are taking an estrogen drug. The science underlying this article is extremely complex. In order to make this information comprehensible to the lay reader, we have made a special effort to translate these new findings about estrogen metabolism into a version that most people will understand.



Nevertheless, some people may have difficulty understanding a few technical areas of this article. This information is so critically important, however, that we urge you to re-read paragraphs you do not understand in order to gain a full grasp of these crucial anticancer concepts.

The word estrogen strikes fear into the hearts of many. Women equate it with breast cancer, scientists equate it with “endocrine disruptors,” and doctors equate it with hormone replacement. Are these perceptions accurate?

Estrogen is many things. It includes the body’s natural estrogenic hormones and things that look like the body’s natural hormones. As long as something behaves like an estrogen in the body, it is an estrogen, or is, quite simply, “estrogenic.” The strongest natural estrogen in the human body is estradiol. Premarin® is an example of an unnatural estrogen—unnatural, at least, to the human body. It is made from estrogens excreted in the urine of pregnant horses. Chemical estrogens that behave badly once they are inside the body are known as “endocrine disruptors” for their adverse effects on development. All of these estrogens interact with the body’s innate hormonal system. They do not, however, provoke the same responses.



Photomicrograph of estradiol crystals. Estradiol, the most potent of the natural estrogens, is used in its natural or semisynthetic form to treat menopausal symptoms.

What Makes Estrogen Tick

“Estrogen receptors” are rarely talked about unless a woman is diagnosed with breast cancer (or a man with prostate cancer), but they are critical to how an estrogen behaves. For example, tamoxifen is a “known human carcinogen” due to its estrogenic effects, yet it is marketed as an “estrogen blocker” because of its estrogen-blocking effects. It has beneficial effects on bone, but negative effects on the circulatory system.^{1,2} It blocks estrogen-driven breast cancer growth temporarily, yet later becomes estrogenic in the same tissue, promoting new breast cancer. How can one “estrogen” do all these things?

The answer is, partly, estrogen receptors, which are proteins in the body that react to estrogen. Estrogen is like fuel, and estrogen receptors are like machines. When fuel meets machine, things happen.

Unfortunately, what happens depends on which area of the body is in question. The receptors of different parts of the body are different. In other words, although all the machinery runs on some type of estrogen, not all the machinery does the same thing. Estrogen does different things in different parts of the body. It does one thing in the brain and another in the breast. It might surprise you to learn, for example, that the pituitary gland is second after the uterus as the most estrogen-responsive area of the body.³ So it is not accurate to think of estrogen as the thing that makes breast cancer cells grow.

Just a few years ago, researchers believed that there were two types of estrogen receptors: alpha and beta. That made things fairly simple. Estrogen hits receptor alpha and Y happens. Research focused mostly on the strong estrogen—estradiol—and it seemed that progress could be made in understanding how estrogen affects at least breast tissue, though strange things continued to happen, such as the estrogen “blocker” tamoxifen causing the growth of tamoxifen-dependent cancers. With the discovery of a much larger picture, those days are over and a lot of research is now out the window. As a researcher at Columbia recently lamented, “where will it end?”⁴ There is more to it than anyone ever imagined.

The Plot Thickens

It has now been discovered that there is an entire new class of estrogen receptors called estrogen-receptor-related receptors. These receptors do not respond to the body's natural estrogen.^{5,6} They are instead activated by xenoestrogens (estrogens from the outside, or from the environment).⁷ Pesticides and tamoxifen are two examples of xenoestrogens that activate estrogen-receptor-related receptors.^{8,9} The extraordinary thing about these receptors is that they represent a whole new class of estrogen machinery, previously unknown. Not only can these receptors do everything the estrogen receptors that respond to "natural" estrogen can do, but they also have a major impact on how an estrogen—any kind of estrogen—behaves.⁶ The discovery of this new class receptors will enable researchers to understand, for the first time, how environmental estrogens ("endocrine disruptors") interfere with the body's normal metabolism, and to better define the use of natural estrogen.

Estradiol Stops Cancer Cell Growth

How can this "strong" hormone—estradiol—stop hormonally responsive cancer cells from multiplying? The answer to that question first appeared in the *Journal of the National Cancer Institute*,¹⁰ and has been known since at least 1977.¹¹ The cancer cells that estradiol stopped from growing had been treated with tamoxifen. Tamoxifen works two to five years after breast cancer treatment to block estrogen and prevent cancer recurrence, and then usually does the opposite.¹²⁻¹⁴ When it starts doing the opposite of what it is supposed to do, so does estradiol. How can this puzzle be solved?

In 2001, researchers reported for the first time that tamoxifen breakdown products interact with one of the newly discovered estrogen-receptor-related receptors, and keeps it from activating certain genes normally activated by estrogen.^{8,15} This opened a whole new vista for understanding how tamoxifen and other synthetic estrogens work. Important clues have already been found.

Estrogen Cofactors Discovered

In addition to interacting with estrogen-receptor-related receptors, tamoxifen and other xeno-estrogens interact with yet another new discovery.

In the laboratory, researchers can get estrogen, by itself, to activate estrogen receptors. In other words, in a laboratory setting, any estrogen fuel will activate the estrogen machinery and set things in motion. In real life, this does not happen. In real life, estrogen is only one of many factors that coordinate as a group to activate estrogen receptors.

The body makes proteins known as "coactivators" and "corepressors." These proteins attach themselves to estrogen and other hormones such as thyroid, creating big, complex "globs." It is these globs—not estrogen alone—that activate or suppress what was previously attributed to estrogen alone. In other words, studies showing what an estrogen does in the laboratory may have little to do with what actually occurs in the human body; in real life, other proteins run the show. This is bold new territory for hormone research.

Here is an example of just how important these coactivator and corepressor proteins are in determining how estrogen behaves. Corepressor SSN6 blocks estrogen's effects in cells. In other words, the SSN6 protein shuts the machinery down. The estrogen fuel can be available (estrogen could be floating all around), but the machinery will not start as long as corepressor SSN6 is working. It neutralizes the effects of estrogen. If something interferes with this protein, however, instead of dampening the effects of estrogen, it enhances them. In addition, estrogen blockers turn into estrogen enhancers.¹⁶ Sound familiar? The importance of coactivators and corepressors cannot be overstated. They interact with both estrogen receptors and the newly discovered estrogen-receptor-related receptors. As you will soon read, there may be natural ways for women to regulate these "coactivators" in a manner that reduces breast cancer risk.

Estrogen Imposters

The three principal types of estrogen manufactured by the human body are estradiol (17 beta-estradiol), estriol, and estrone. Estradiol is the most feared because it is the strongest and is associated with the growth of cancer cells. Estrone is a metabolite of estradiol, and is less potent. Estriol is another metabolite, but is considered so mild mannered that it is recommended as a safe hormone replacement.¹⁷⁻¹⁹ In addition, the human body contains 11 other estradiol metabolites that hardly anyone ever mentions.

Premarin® and Prempro™ are drugs made of 17 beta-estradiol and more than a dozen estrogen metabolites from horses.²⁰ These manmade drugs should not be confused with any estrogen manufactured by the human body, with other estrogen drugs, or with estrogen in general. The data from studies of women taking these drugs cannot, and should not, be extrapolated to other hormone replacement drugs or therapy. This is an important point: Premarin® is not estrogen, but instead is an estrogen—one of many estrogens. Different estrogens produce different effects. The manufacturer of Premarin® and Prempro™ has argued that its horse estrogens have unique effects in humans, and undoubtedly they do.



Dozens of studies demonstrate important differences between the effects of Premarin® on the human body and the effects of other estrogen products. Transdermal estradiol, for example, may decrease triglycerides and LDL oxidation, whereas Premarin®

may do the opposite.²¹ Premarin® may increase C-reactive protein (a negative for the heart) while transdermal estradiol may not.²² Changing from Premarin® to transdermal estradiol may reduce triglycerides significantly.²³ Estrogen patches may reduce blood pressure, whereas oral estrogen may not.²⁴ These and dozens of other studies show different effects depending on which estrogen drug is being evaluated. Not only are there differences between Premarin®/Prempro™ and other drugs, but there are differences between other drugs as well.



Neutralizing Estrogen: The Asian Advantage

Japanese women have been reported to have higher levels of estradiol in their blood than Americans, yet they have a much lower risk of breast cancer.^{25,26} Why? Researchers believe it has more to do with environmental factors than genetics. When Japanese and other Asians adopt a Western lifestyle, risk increases.^{27,28} The Asian diet may contain things that modulate the response to estrogen, and strong evidence indicates that how the body handles estrogen is far more important than how much estrogen it handles. Research indicates significant differences between Japanese and Western women in their number of estrogen receptors and in their response to xenoestrogens.²⁹⁻³¹ These differences suggest the involvement of the newly discovered estrogen coregulators. Dietary factors can activate or deactivate these factors, which means that every

woman can regulate her own estrogen, to a certain extent.

Researchers have extensively investigated three aspects of the Asian advantage: soy, vegetables, and green tea. Each is associated with a dramatically lower risk of breast cancer.

Drinking 36 ounces of soy milk a day can reduce levels of estradiol by 20-27% within weeks.^{32,33} Soy contains isoflavones that neutralize “strong” estrogens, converting them to estrogen metabolites that protect against breast cancer.³⁴ When mice implanted with human breast tumors were given soy concentrate and green tea, tumor size was reduced by 72%.³⁵ Estrogen receptor alpha was also reduced, an indication that the combination of soy and green tea was working at the genetic level, probably with estrogen cofactors. Forty milligrams of isoflavones a day significantly decreased “strong” estrogen levels in women, according to a study from the H. Lee Moffitt Cancer Center in Tampa, FL.³⁶ These are only a few of the many studies demonstrating the beneficial effects of soy.

In another experiment that shows the hormonal benefits of soy on the effects of chemical estrogens, when female monkeys were given birth control pills, their cortisol shot up, and their DHEA and testosterone plummeted. When they were given Premarin®, the same thing happened. When the monkeys were given soy protein with isoflavones, however, their hormones normalized.³⁷

Several years ago, there was concern about genistein, an isoflavone in soy, when research showed that it activated estrogen-related genes. Some people took this to mean they should avoid consuming soy, which would be unfortunate given the overwhelmingly positive data about soy’s benefits to humans. Genistein has been called the “good estrogen” for its beneficial effects against estrogen-responsive breast cancer.³⁸ It subsequently emerged that most of the negative research on genistein was generated by one researcher, under conditions that would not exist in real life (such as extremely high levels of genistein put into cancer cells that were deprived of all other estrogen).

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The human body manufactures estrogen as a necessary component in many processes; estrogen is always in the body, even in postmenopausal women. Copper, too, is always in the body and is another example of something that can distort the way genistein behaves in a test tube.³⁹ Researchers at the University of California, Davis, recently did the same test tube study on genistein and produced the same negative results. They then put genistein in a test tube with the cancer cells and environmental estrogens. The result showed that genistein suppressed cancer cell growth.⁴⁰ These studies on pure genistein, however, do not accurately reflect what occurs in a complex environment such as the human body.

Fortunately, the safety of soy isoflavones (including genistein) for human consumption has been confirmed by experiments with monkeys, the experimental model closest to humans.⁴¹ Monkeys treated for three years with soy or soy minus its isoflavones exhibited no abnormal cell growth; in fact, the result was just the opposite. The researchers concluded, "These findings suggest that high dietary levels of soy isoflavones do not stimulate breast or uterine proliferation in postmenopausal monkeys and may contribute to an estrogen profile associated with reduced breast cancer risk." In addition, a new study clarifying the estrogenic effects of genistein on the uterus found that genistein may enhance cell growth for a few days, but then the effect stops. This is a new finding, and the results are different from those for estrogen drugs that perpetuate growth indefinitely.⁴² With any luck, issues surrounding how genistein behaves will be soon resolved.

It is important to remember that genistein also blocks the growth of estrogen-receptor-negative breast cancer cells. By incorporating soy and isoflavones in her diet, a woman can potentially stop breast cancer before it develops.⁴³ The one caveat is that genistein may interfere with tamoxifen, and thus should not be taken by itself with that drug.⁴⁴

One of the most exciting new findings is that genistein keeps amyloid from killing brain cells (without any negative effects on uterine cells), and has been suggested as an alternative to synthetic estrogens for the prevention of Alzheimer's disease.⁴⁵ Studies of the popular estrogen drugs Premarin® and Prempro™ show that they may actually increase the risk of dementia.⁴⁶

Everybody knows that vegetables are good for you, and they are especially good for women who want to avoid breast cancer. Vegetables enable the body to rid itself of excess estrogens. Meat eaters have about 50% more estradiol and estrone in their blood than do vegetarians.⁴⁷ Women who eat the most vegetables, beans such as lentils, and fiber reduce their risk of breast cancer risk by 50%.⁴⁸ As you will read next, compounds found in vegetables favorably affect the way estrogen behaves in the body.

Other Ways To Tame Estrogen

The way estrogen is metabolized is critical to how it behaves. Fortunately, we can do more than cross our fingers and hope for the best. Certain compounds found in plants turn harmful estrogen into a more beneficial version. Chief among them is indole-3-carbinol (I3C), a phytochemical found in cruciferous vegetables such as broccoli. In China, where the risk of breast and prostate cancers is minuscule, consumption of cruciferous vegetables is more than three times that of the US.⁴⁹

I3C helps convert "strong" estrogens into benign or even helpful estrogens such as 2-hydroxyestrone.^{50,51} It also acts very much like tamoxifen in blocking undesirable estrogenic effects in breast cancer cells, and its antiestrogen effects are enhanced with genistein.⁵²



When digested, I3C is converted to other substances, including diindolylmethane (DIM). Some earlier research suggested that I3C's beneficial effects were due to DIM. New research shows this is not the case, and that there are important differences in the effects of I3C and DIM on the metabolism of estrogen. Researchers recently stated, "This finding [of I3C's effects] is inconsistent with the claim that DIM is the biologically active metabolite of I3C with regard to its antiestrogenicity." DIM does not increase beneficial 2-hydroxylation of estrogen (at least in rats), but it does lower harmful 4- and 6-hydroxylations.⁵³ By contrast, I3C, which partially converts to DIM during digestion, affects all three in a positive way. Moreover, DIM does not have the anti-estrogen effects of I3C.⁵⁴

Another potential supplement for breast cancer prevention that has drawn a lot of interest is melatonin. Melatonin is associated with sleep because it builds up during the night, but it may ultimately end up being more associated with estrogen than with sleep. Studies show that melatonin plays a major role in how estrogen behaves. In estrogen-receptor-positive breast cancer cells, melatonin can bring cell growth to a halt.⁵⁵ Research indicates that melatonin controls estrogen, and vice versa.⁵⁵⁻⁵⁷ In studies of rodents, melatonin shows great promise with regard to its ability to prevent breast cancer when given continuously, before and after exposure to a carcinogen, and when given to mice with the HER2/neu genetic alteration.^{58,59} Researchers have been unsuccessful in correlating blood levels of melatonin with breast cancer.⁶⁰ This reflects melatonin's complexity as a hormone

that, like estrogen, comes in various forms and has several receptors. Without a doubt, melatonin plays a major role in breast cancer through its effects on estrogen and other cancer-related phenomena.

As an antioxidant, melatonin is not only powerful but also unique. Unlike vitamin E, which essentially has no further effects after it scavenges a radical, when melatonin gets a radical, it creates a new melatonin antioxidant; that is, it self-perpetuates. It also cooperates with other antioxidants like vitamins C and E.⁶¹ Antioxidants are very important in preventing cancer, and it has been reported that free radicals can activate or deactivate genes that are involved in breast cancer.⁶²

In addition, melatonin may suppress cortisol, which is a stress-related hormone.^{63,64} It is interesting to note that the overwhelming majority of breast cancer patients say stress caused their disease.⁶⁵ In a study of older women, 2 mg of melatonin per day reduced estradiol levels, enhanced sleep, and improved levels of DHEA.⁶⁶ Melatonin is very potent, and as little as 0.3 mg per day may be enough to produce beneficial effects.



Breast cancer is a serious concern for most women. Understanding that there are different types of estrogen, that different estrogens have different effects, and that women can, to a certain degree, control their own estrogen (through dietary modification and supplement use) will help women make informed choices about estrogen exposure and reduce their risk of breast cancer. Recent discoveries about estrogen receptors and how they interact may finally unlock the mysteries of how estrogens work, and provide the basis for nontoxic treatment and effective prevention.

What Causes Breast Cancer

According to the Breast Cancer Fund, a woman's risk of contracting breast cancer was 1 in 22 in the 1940s. Today, it is 1 in 7. There is no end to the theories as to why this risk has increased. "Endocrine disruptors" (chemicals that mimic hormones) are a likely suspect. They are wreaking havoc on wildlife and clearly affect brain cells in the developing embryo.⁶⁷ So far, however, studies have failed to show a link between breast cancer and blood levels of these chemicals. Still, they remain suspect—especially in combination with other factors.

Mainstream dogma is that exposure to estrogen causes breast cancer. By "estrogen," the mainstream means the body's own estrogens. This line of thinking always links variables (such as having/not having children or the age at which menopause occurs) to estrogen exposure and, hence, breast cancer risk. While this viewpoint appears to have some validity, a few things are wrong with it, including the thorny question of why, all of a sudden, exposure to something that has been a part of the human body for eons would cause cancer. It also skirts the question of why long-term use of birth control pills containing estrogens does not increase the risk of breast cancer.⁶⁸

Genes are another possible explanation for breast cancer. This depressing theory implies that whether or not people get breast cancer is beyond their control and that nothing can be done about it, except having the breasts removed as a preventive measure.⁶⁹ New research may put an end to the notion that there is nothing a person can do about "bad genes."

"Bad genes" do not necessarily come from parents. Sometimes they come from the environment. Eighty-five percent of the "family risk" for breast cancer may come from something besides an inherited gene.⁷⁰ Moreover, it has now been discovered that there are genes that can modify "bad genes."^{71,72} In other words, you may not have to live with "bad genes."

In addition, a new study shows that even if a person has a genetic predisposition toward breast cancer, the cancer does not necessarily activate unless the person encounters something in the environment that activates it.⁷³ For some women, that "something" could be meat. For the first time, eating meat has been linked to genes and breast cancer.⁷³ Families tend to share not only genes but recipes as well, and it is becoming clear that what you eat may be more important than what you were born with.

In studies that search for the cause of breast cancer, certain things consistently emerge. One is that diets rich in vegetables, soy, and green tea reduce cancer risk, and diets rich in animal fats (especially from red meat) increase risk.⁷³⁻⁷⁹ In a study from the Barbara Ann Karmanos Cancer Institute at Wayne State University in Detroit, beef, pork and vegetables accounted for 85% of the alterations to DNA in women, with meat causing damage and vegetables preventing it.⁸⁰ Damaged DNA lays the groundwork for cancer.



The case of red meat is interesting not only because cooking it creates carcinogens, but also because the use of hormone implants in cows (which dates back about 50 years) coincides with the beginning of a major increase in breast cancer in North America.⁸¹ Countries with the highest rates of breast (and prostate) cancer also are the countries that allow such implants. North America's breast cancer rate is the world's highest—higher than all of South America and northern and southern Europe combined.⁸² Australia and New Zealand, which allow hormones to be implanted in cattle, have similarly high rates of breast cancer. In Europe, such implants are banned.

It is not hard to figure out why. Cattle implants contain 17 beta-estradiol and other strong steroids, including synthetic estrogens. Cows are repeatedly implanted, and the implants are in the cows when they are slaughtered. Guidelines published by the US Department of Agriculture and the University of Nebraska advise implanting the strongest drug last, 70 days before slaughter.⁸³ The strongest implants last 90-120 days. Besides being in the cows at the time of slaughter, over time the hormones build up in fat.⁸⁴ Fifty percent of the hormones contained in a steak may be in the fat.⁸⁴ Neither the FDA nor the USDA monitors the use of hormone implants, or tests for residues in beef. Testing for the metabolites of estradiol alone would be a major undertaking, as there are more than a dozen such metabolites, and this is just one estrogen. Cows are given other hormones as well, including "male" hormones. Heifers are fed melengesterol acetate, a synthetic progesterone used for birth control and promoting rapid weight gain.

It has been demonstrated that a diet high in beef fat activates hormone-related genes.⁸⁵ Zeranol, a synthetic estrogen cow implant, causes breast cancer cells to grow in the test tube. The amount of Zeranol needed to cause this growth is 30 times less than the amount that the FDA deems to be safe.⁸⁶ A follow-up study being conducted at Ohio State University hopes to ascertain how much Zeranol ends up on the dinner plate and in the tissue of women with breast cancer.⁸⁷ The study, which began in 2002, is still in progress. Data from approximately 200 women have been collected and are being analyzed. This important study may shed some light on at least one hormone implant. Studies on the total amount of all hormones added to American beef have yet to be conducted.

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What Women May Consider After Breast Cancer

“Stop taking estrogen” are usually the first words out of a doctor’s mouth after telling a woman that she has breast cancer. The estrogen that she is most likely to be taking is Premarin® or Prempro™ drugs associated with a 300% increased risk of breast cancer.⁸⁸ Doctors equate Premarin® with estrogen, and estrogen with breast cancer. But hold on a minute—must a woman who has had breast cancer necessarily live the rest of her life in an estrogen-deficient state because one drug might have caused problems?

Not according to the research. In fact, a study from the Fred Hutchinson Cancer Research Center in Seattle showed a 50% reduction in the recurrence of breast cancer in women who used hormone replacement therapy, regardless of whether the therapy was oral, local, or both.⁸⁹ Doctors at Chicago’s Rush-Presbyterian-St. Luke’s Medical Center have argued for a change in viewpoint on the subject. Researchers at the MD Anderson Cancer Center in Houston have been examining the question for more than a decade,^{90,91} and have found no compelling evidence against the use of hormone replacement therapy following breast cancer treatment.

In a study from the University of Texas Southwestern Medical Center in Dallas of 64 women with previous breast cancer—some of which was estrogen receptor positive—one case of recurrence and one case of new cancer in the other breast was reported after an average time on replacement therapy of 6 years and follow up of 12 years.⁹² Researchers concluded that the use of hormone replacement therapy is not associated with increased breast cancer.

No large, long-term studies have been conducted, but two reports on all the smaller studies both state that there is no increased risk of recurrence or new cancer in the opposite breast—receptor positive or negative.^{93,94}

Premarin® and Prempro™ do not appear to have the same propensity to promote breast cancer following treatment. A report from the University of California, Irvine, found 13 recurrences in 145 women taking Prempro™ for an average of 2.5 years after treatment for breast cancer.⁹⁵ Another report from South Africa had similar results. In 20 women taking Prempro™ and 4 taking tibolone (another hormone replacement drug), no recurrences were reported after three years of observation.⁹⁶ This contrasts sharply with the more than four times increased risk for breast cancer in women taking tibolone, and almost three times increased risk in women taking Prempro™, reported for women who have never been treated for breast cancer.⁹⁷

At this time, no compelling published evidence exists to suggest that taking hormone replacement therapy after treatment for breast cancer increases the risk of recurrence or new cancer in the other breast. Some caveats should be noted, however. Large, long-term studies have not been conducted, and until they are, nothing is definite. Second, important differences exist between hormone replacement therapies. For example, in one study, the drug Prempro™ caused significant breast density in 40% of women; by contrast, oral low-dose estrogen caused it in 6%, and transdermal estrogen in 2%.⁹⁸ Breast density increases the chance that a mammogram can be misread.

Another overlooked factor in these studies is that when women survive breast cancer, they change their habits. In one study, 77% reduced their consumption of meat, and 72% increased their intake of fruit and vegetables.⁹⁹ In another study, 64% started using dietary supplements, and almost all reported benefits.¹⁰⁰ Women who have completed breast cancer treatment are seven times more likely to use alternative therapies, and if they are taking tamoxifen, they are even more likely to use alternative therapies to alleviate symptoms, with soy being a top choice.¹⁰¹

Might these changes in diet and lifestyle change a woman’s risk/estrogen profile so that a xenoestrogen such as a hormone replacement drug might behave differently in her body? It is very likely, in view of scientific studies showing how various dietary factors modulate estrogen. In addition, breast cancer treatment may permanently alter the genes that respond to estrogen. Contradicting this, however, are short-term studies showing that breast cancer patients who take estrogen-suppressing drugs (aromatase inhibitors) have a reduced risk of cancer recurrence. None of these studies, however, looks at lifestyle modifications that could skew the findings. In other words, the women whose breast cancer did not recur when taking aromatase inhibitors could have made significant improvements in their diets that were not accounted for in these studies. These dietary changes, and not the estrogen-suppressing drug, could be responsible for the cancer not recurring.

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