Medically Reviewed

Do Fertility Drugs and IVF Increase Breast Cancer Risk?

If you're worried about the side effects of high estrogen during IVF, you can relax, say experts. Here's why.

Updated May 22, 2023 By: Barbara Brody Medical Reviewer: Maryam Lustberg, M.D., M.P.H., director of the breast center, chief of breast medical oncology



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If you're struggling to conceive and are going through or considering fertility treatments, you might worry about the effects of hormone-altering medications. After all, prolonged exposure to the female reproductive hormones estrogen and progesterone is linked to a higher breast cancer risk.

Fortunately, taking fertility drugs or undergoing in-vitro fertilization (IVF) won't increase your chance of developing <u>breast cancer</u>, says <u>Kandice K. Ludwig, M.D.</u>, the medical director of the breast program at the Schwarz Cancer Center at Indiana University Health North Hospital in

Carmel. "The notion [that fertility treatments increase breast cancer risk] has been disproven," she says.

IVF and Breast Cancer

Can IVF Cause Breast Cancer? What the Research Says

Over the years, many studies have tried to determine whether there is a connection between using fertility drugs and treatments like IVF and an increased risk of breast cancer. The best evidence to date suggests that there is not, says Dr. Ludwig.

In a 2022 meta-analysis on fertility treatment and breast cancer published in the journal *BJS Open*, researchers conducted an extensive review of all research published over a 20-year timespan related to fertility treatments (also called assisted reproductive technology) and breast cancer. The authors, who analyzed 24 studies that included a total of nearly 620,000 participants, adjusted for possible confounding factors that were present in any of the included studies. For example, older age may be a confounding factor, because women who have their first baby after the age of 30 have a higher risk of breast cancer compared to those who give birth at a younger age, according the National Cancer Institute.

After completing the analysis, the researchers determined that there "was no significant breastcancer risk association with fertility treatment." They even checked to see whether undergoing many (six or more) IVF cycles would increase the risk of breast cancer; it did not.

The authors also explored the possibility that specific types of medications that are frequently used during fertility treatments might increase breast cancer risk, but no such link was found. According to their analysis, there was no increased risk of breast cancer associated with the use of Clomid (clomiphene, a drug used to induce ovulation), human chorionic gonadotropin (HCG injections, which stimulate the release of eggs), gonadotropin analogues (sometimes used in women with <u>endometriosis or fibroids</u>), or progesterone (a hormone which supports embryo implantation).

Confusion Around It

Confusion About IVF, Infertility, and Breast Cancer Risk

You'd think a review of two dozen studies spanning two decades, yielding solid evidence that <u>fertility</u> treatments do not cause breast cancer or increase cancer risk, would settle the question once and for all. So why do some people still assume there's a risk?



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In part, because there are complexities in the research: For instance, some studies suggest that women who undergo fertility treatments might be slightly more likely to develop certain kinds of breast cancer than those who do not, as noted in a <u>2021 review article from Iranian researchers</u>. However, the fertility treatments themselves are probably not to blame, says <u>Paula C. Brady</u>, <u>M.D.</u>, a reproductive endocrinology and infertility specialist at the Columbia University Fertility Center in New York City.

Any data suggesting that fertility treatments increased the risk of breast cancer "is confounded by the fact that infertility itself is associated with an increased risk of breast cancer," says Dr. Brady. "Infertility is a medical condition, and it has ramifications. Patients with infertility have an increased risk of cardiovascular disease, and they also have an increased risk of birth defects in their pregnancy." They're also more likely than women who don't experience infertility to get breast cancer, but that holds "whether they do fertility treatment or not. The risks are already present."

Why infertility itself seems to raise the risk of breast cancer isn't totally clear, but underlying health conditions may play a role. For instance, women who require fertility treatments to get pregnant are also more likely to have <u>dense breasts</u>, according to 2016 study published in <u>Breast Cancer Research</u>, and women with <u>dense breasts</u> have a higher risk of developing breast cancer, according to the Centers for Disease Control and Prevention (CDC).

In addition, women who <u>seek out</u> fertility treatments <u>tend to be older</u>, and breast cancer risk goes up with age. In fact, a new study published in <u>Breast Cancer Research and Treatment</u> concluded that being older at the time of a first birth is a major reason why infertility and breast cancer are linked.

According to the <u>National Cancer Institute</u>, a 30-year woman has a one in 204 chance of developing breast cancer in the next 10 years; by age 40, a woman's risk of breast cancer in the next decade jumps to one in 65. And older women are more apt to have trouble conceiving

naturally. According to <u>the CDC</u>, about 37% of people using assisted reproductive technology (ART) are younger than 35. The overwhelming majority are age 35 or older, and more than 20% of ART users are at least 41. That means women are more apt to be getting infertility treatments at a time when their breast cancer risk is starting to climb because of their age.

Impact of Estrogen

Does Estrogen or Estradiol Impact Breast Cancer Risk?

Some people worry that too much estrogen or estradiol (the <u>most potent type</u> of estrogen, often used in IVF) can lead to breast cancer, and it's true that using fertility treatments may raise hormone levels dramatically. In addition to taking supplemental estrogen or estradiol, many women using a variety of fertility treatments take other drugs, such as Clomid (clomiphene), that result in increasing natural production of estrogen. However, there's a difference from being exposed to excess estrogen for a long period of time and just raising your levels briefly in order to promote conception and a healthy pregnancy, says Dr. Brady.

"Exposure to our naturally occurring hormones ultimately fuels risk of breast cancer," she says, explaining that women who start having periods at a very young age or reach <u>menopause</u> at a later than average age have a higher risk of breast cancer.

What's more, <u>women who have given birth</u> have a lower risk of breast cancer compared to those who have never birthed a baby, she says, meaning that pregnancy itself—which for some women is not possible without fertility treatments such as IVF—is somewhat protective.

Elevated BC Risk and IVF

What if You're Already at High Risk for Breast Cancer?

Women who have an elevated breast cancer risk—perhaps because of their family history or a genetic mutation—can still safely use fertility treatments, including IVF, says Dr. Brady. "I also see patients who have had breast cancer and want to be pregnant afterwards." Breast cancer survivors who use fertility treatments <u>don't have a higher risk of breast cancer recurrence</u>, she says.

That said, if your doctors think you should start breast cancer screening early (for example, if you have a <u>family history of breast cancer</u>), it's wise to get screened before trying to get pregnant, especially if you have any reason to believe that your risk of cancer is heightened. If you're a candidate for testing to check for a gene mutation that greatly increases breast cancer risk, consider getting tested first, says Dr. Brady. If it turns out that you have a BRCA or other cancer-

related gene mutation, she strongly advises talking to your fertility specialist about PGTM, or preimplantation genetic testing for a monogenic disease.

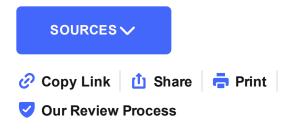
PGTM entails screening embryos for a disease-causing gene that either parent carries and only implanting the embryos that lack this mutation during IVF in order to avoid passing it on to your offspring.

Whether you get pregnant naturally or with the help of modern medicine, you should also know that it's possible to develop breast cancer while you're pregnant, even if you don't have a family history or genetic mutation that raises your risk.

"We do see women who get diagnosed while they're pregnant or <u>breastfeeding</u>," says Dr. Ludwig. That's why it's important to bring any changes you notice to the attention of your doctor right away. "Most of the time, a lump during breastfeeding is a clogged duct, but sometimes it's not." Either way, if it turns out to be breast cancer, now you know: IVF is not to blame.

This article was originally published April 24, 2023 and most recently updated May 22, 2023.

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