

# Cancer Association of South Africa (CANSA)



## CANSA Fact Sheet on Contraceptive Choices and Fertility Options for Women Diagnosed with Breast Cancer

### Introduction

Often, pregnancy after cancer treatment is safe for both the mother and baby. Pregnancy does not seem to raise the risk of cancer coming back. Still, some women may be told to wait for a number of years before trying to have a baby. How long depends on several factors:

- The type of cancer and stage
- Type of treatment received
- The woman's age



[Picture Credit: Fertility Options]

Reproductive-aged breast cancer survivors have many unique considerations when making decisions about contraceptives, which may put them at risk for choosing methods that do not align with their reproductive goals. Hormonal contraceptives are contraindicated for survivors during the first five years after breast cancer regardless of hormone receptor status. Additionally, breast cancer survivors with specific types of breast cancer are commonly prescribed endocrine therapy for five or more years, during which pregnancy is contraindicated due to tamoxifen's teratogenic effects. Previous studies have found that some cancer survivors believe that they are incapable of becoming pregnant, fail to use any contraceptives or use less-effective contraceptives, which puts them at risk for an unintended pregnancy.

According to Cancer Research UK, some chemotherapy drugs are more likely than others to cause infertility. Infertility means one cannot get pregnant. Whether the infertility is temporary or permanent depends partly on the drugs one receives and the dose. One should ask one's treating physician if the drugs one is receiving are likely to make one infertile. Permanent infertility is more likely if one has higher doses of the drugs. It is also more likely in older women than younger women – especially if one is getting close to the age where one would naturally reach menopause. Some chemotherapy drugs can be very damaging to the eggs in one's ovaries, so that none are left after treatment. If this happens, one can no longer get pregnant, and one might have symptoms of menopause.

Contraception is challenging for women with cancer, particularly those with breast cancer, who are limited to long-acting non-hormonal methods, the copper T380A intrauterine device (IUD), as hormonal contraception is contraindicated and discontinued in women with breast cancer. Given the recommendations to avoid pregnancy and hormonal contraceptives as well as the reduced number of contraceptives available to breast cancer survivors, contraceptive counselling that is tailored to each woman's needs, concerns and cancer

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history would be ideal. Currently, these women may be only receiving contraceptive counselling to avoid hormonal methods but may not be getting additional counselling about methods that are effective and consistent with individual desires. It is imperative that breast cancer survivors receive accurate counselling to help them make informed contraception decisions. Little is known about breast cancer survivors' contraceptive counselling preferences. Any insight into these topics will help inform patient-centred care and potentially decrease the incidence of unintended pregnancy in this population. Contraceptive counselling has the potential to facilitate the selection of safe contraceptives, assist women in making decisions around when to consider future childbearing, and can prevent unintended pregnancy across the cancer care continuum.

Many women are able to become pregnant after being treated for breast cancer. However, some breast cancer treatments can make it harder to fall pregnant. If one thinks that one might want to have children one day, or just want to keep one's options open, the best time to talk to a doctor about this is **before** beginning breast cancer treatment. The same may apply to other cancer treatment(s) as well.

Some treatments for breast cancer might affect a woman's fertility. For example, chemotherapy for breast cancer may damage the ovaries, which can sometimes cause immediate or delayed infertility. Still, many women are able to become pregnant after cancer treatment.

If the fertility concern is about the potential father undergoing cancer treatment, it is generally believed that men can try to conceive a child after their cancer treatment ends. There appears to be no firm rules for how long men should wait after cancer treatment, although health care providers usually recommend waiting 2 to 5 years. Although sperm may be damaged by chemotherapy or radiation therapy, those sperm should be replaced in about 2 years. Should it, however, happen that a child is "accidentally" conceived soon after the father's cancer treatment ends, there is currently no research showing that the foetus will have a greater risk of developing serious health problems.

### **Pregnancy and Cancer with a Focus on Breast Cancer and Pregnancy**

When women find out they have breast cancer, many leave their obstetrician-gynaecologist and go to a cancer specialist (Oncologist). After treatment, they usually return to their obstetrician-gynaecologist. Although their breast cancer may be gone, their cancer-related health issues remain. Concerns about fertility, contraception, menopause, and bone health are common.

Breast Cancer survivors can have both short-term and long-term side effects. These include:

- Hot flashes
- Vaginal dryness
- Osteoporosis
- Premature menopause
- Loss of fertility
- Body image problems
- Sexual problems, including dyspareunia (painful sex)

Most doctors advise women that it is best to wait for 2 years (or longer) after breast cancer treatment, before getting pregnant. This is because breast cancer is most likely to come back within the first 2 years after one was first diagnosed with breast cancer. Having treatment for breast cancer that has come back could be difficult if pregnant or if one has a young baby. However, most studies have found that pregnancy after treatment for breast cancer does not increase the risk of cancer coming back.

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## How Cancer Drugs Affect Female Fertility

Female fertility may be affected by various cancer treatments (and age) which may include:

### Chemotherapy

At birth each female is born with the eggs (ova) that she will have throughout her life. Once puberty commences, hormones are released which allow mature eggs to be released every month during the menstrual cycle until menopause is reached. Once the normal hormonal cycle is interrupted, the female will go into menopause. Hormones, like oestrogen, is needed to release mature ova (eggs) each month. Oestrogen also prepares the uterus to receive a possibly fertilised ovum (egg). Oestrogen is manufactured in the quickly dividing cells of the ovaries.

Chemotherapy drugs has its effects on quickly dividing cells, thereby, affecting the quickly dividing cells in the ovaries. Hence a negative effect on female fertility. The effect of some chemotherapy drugs may even cause a woman to reach early menopause.

Whether or not female fertility is affected by chemotherapy drugs depends on factors such as:

- One's baseline fertility
- One's age at the time of treatment
- The type of cancer and treatment(s)
- The stage of the cancer
- The amount (dose) of treatment
- The length (duration) of treatment
- The amount of time that has passed since cancer treatment
- Other personal health factors
- Genetic factors
- Whether one has an underactive thyroid after cancer treatment

Chemotherapy drugs that may possibly affect fertility in females include (in alphabetical order – the list may not be complete. It must be noted that not all of these drugs are available or used in South Africa):

- 5-fluorouracil
- Bleomycin
- Busulfan
- Carboplatin
- Carmustine
- Chlorambucil
- Cisplatin
- Cyclophosphamide
- Cytarabine
- Cytosine arabinoside
- Daunorubicin
- Doxorubicin
- Ifosfamide
- Lomustine
- Melphalan
- methotrexate
- Mitomycin-C
- Nitrogen mustard (mechlorethamine)
- Procarbazine
- Temozolomide
- Thiotepa
- Vinblastine
- Vincristine

### Radiation Therapy

Radiation therapy uses a controlled dose of radiation to kill cancer cells or damage them so they cannot grow and multiply. It can be delivered from inside (brachytherapy) or outside (external beam radiation) to the body.

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The risk of infertility will vary depending on the area of the body that is treated, the dose of radiation and the number of treatments.

- Radiation therapy to the pelvic area (for cancer of the rectum, bladder, cervix, uterus, or vagina) can stop the ovaries producing hormones. This results in temporary or permanent menopause. If one's ovaries do not need treatment, one or both may be surgically moved higher in the abdomen and out of the field of radiation. This is called ovarian transposition or relocation (oophoropexy), and it may help the ovaries to keep working properly.
- Radiation therapy to the pelvic area can also affect the uterus, make sexual intercourse uncomfortable, and increase the risk of miscarriage, premature birth, and low birth weight.
- Radiation therapy to the brain may damage the pituitary gland, which releases hormones that tell the ovaries to release an egg each month which may affect ovulation.

The risk of infertility may increase if one is treated with both chemotherapy and radiation therapy (chemoradiation).

### Surgery

Surgery that removes part, or all of the reproductive organs, such as the ovaries, fallopian tubes, uterus, and cervix, can cause infertility.

*Removal of the ovaries (oophorectomy)* – if both ovaries are removed (bilateral oophorectomy), you will experience early menopause. You will no longer have periods or be able to become pregnant naturally. If only one ovary is removed, the other should continue to release eggs and produce hormones. You will still have periods and may be able to become pregnant if you still have a uterus.

*Removal of the uterus and cervix (hysterectomy)* – this may be used to treat gynaecological cancers, such as cancer of the cervix, ovary, uterus, and endometrium (lining of the uterus), and sometimes, cancer of the vagina. After a hysterectomy, you will be unable to carry a pregnancy and your periods will stop. As your ovaries will continue to function, you may be able to fertilise your eggs through in vitro fertilization and use a surrogate to carry the pregnancy.

### Hormone Therapy

The hormones oestrogen or progesterone may help some types of breast and uterine cancers to grow. Hormone therapy, as a form of cancer treatment, aims to slow down the growth of these cancers by lowering the amount of hormones the tumour receives.

Hormone therapy can be used for a short time or long term. As it blocks the hormones that are required for fertility, you will have to wait until hormone therapy is finished to try to fall pregnant. One may be able to store eggs or embryos before starting hormone therapy.

Anti-oestrogen drugs (such as tamoxifen and aromatase inhibitors) are used to reduce the risk that oestrogen-sensitive breast cancers will come back after treatment. Many anti-oestrogen drugs are taken for several years. During this time, pregnancy should be avoided, as there is a risk the drugs could harm an unborn child. These drugs do not cause infertility and do not damage the ovaries or eggs. Although hormone treatments for breast cancer are used for many years, it is often possible to take a break from the drugs to try for a baby.

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If you are on hormone therapy and want to become pregnant, talk to your treatment team or fertility specialist about the advantages and disadvantages of stopping hormone therapy.

### Other Cancer Treatments

*Stem cell transplant* – high-dose chemotherapy and, possibly, radiation therapy are given before the transplant to kill the cancer cells in the body. The risk of permanent infertility after high-dose chemotherapy and/or radiation therapy is high.

*Immunotherapy and Targeted Therapy* – the effects of these newer drugs on fertility and pregnancy can vary depending on the drug one is given. It is important to discuss the potential impact of these newer drugs with one's treating physician, Oncologist, or fertility specialist.

### Age

Age is also an important factor, more so for women than for men. Women who are older are more likely to go into an early or permanent menopause (the stopping of monthly periods) from their treatment, than younger women, thus making pregnancy more difficult.

### **Fertility Options for Breast Cancer Survivors**

Currently, there are several potential options, including all available assisted technologies. While there are these options. In South Africa these options are only for women who can access and afford fertility treatment options and are not available in the public sector, and, if they are, there are long waiting periods making this option not feasible for many women. For those women who access fertility treatment, options include:

*In Vitro Fertilization* - In vitro fertilization (IVF) is a complex series of procedures used to help with fertility or prevent genetic problems and assist with the conception of a child.

During IVF, mature eggs are collected (retrieved) from ovaries and fertilized by sperm in a laboratory. Then the fertilized egg (embryo) or eggs (embryos) are transferred to a uterus. One full cycle of IVF takes about three weeks. Sometimes these steps are split into different parts and the process can take longer.

IVF is the most effective form of assisted reproductive technology. The procedure can be done using a couple's own eggs and sperm. IVF may also involve eggs, sperm, or embryos from a known or anonymous donor. In some cases, a gestational carrier - someone who has an embryo implanted in the uterus - might be used.

*Embryo Transfer* - The embryo transfer procedure is the last one of the in vitro fertilization (IVF) process. It is a complex procedure. The entire IVF cycle depends on delicate placement of the embryos at the proper location near the middle of the endometrial cavity – with minimal trauma and manipulation.

- The importance of proper embryo transfer technique for successful IVF cannot be overstated
- Ultrasound guided embryo transfer is the most efficient technique currently available

For IVF, the woman is stimulated with injectable medications to develop multiple eggs. Eggs develop in follicles in the ovaries. When the follicles are mature, the egg retrieval procedure removes eggs from the ovaries. Sperm is added to the eggs and the next day the eggs are checked for evidence of fertilization. An appropriate number of embryos are transferred to the uterus several days later – using ultrasound guidance for best placement.

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*In Vitro Maturation* - In Vitro Maturation (IVM) is a procedure that involves the collection of immature oocytes (eggs) from growing antral follicles from minimally stimulated or unstimulated ovaries. These oocytes are within cumulus-oocyte-complexes (COCs) that are then matured in a laboratory setting prior to being cryopreserved (storing at a very low temperature) or fertilized. Immature oocytes can be aspirated in vivo from unstimulated or mildly stimulated ovaries, and live birth incidences using IVM-derived eggs have been reported upwards of approximately 40% per procedure. IVM can also be performed ex vivo in combination with ovarian tissue cryopreservation. In this case, preparation of the harvested ovarian tissue into cortical strips disrupts small antral follicles in the medulla, releasing COCs that can be used for IVM. This approach has been used to generate additional mature eggs from females (before puberty and adult), which otherwise would have been discarded as part of standard ovarian tissue cryopreservation, and ongoing pregnancies have been reported. Although the initial reports of IVM are promising, overall understanding of the quality and reproductive potential of gametes that did not reach full maturity in vivo is lacking. This lack of knowledge is even more pronounced for prepubertal females and needs further study.

*Oocyte and Embryo Cryopreservation* - embryo and egg freezing require 12 to 14 days for us to stimulate the follicles in the patient's ovaries to produce multiple eggs. This process is called controlled ovarian stimulation, and it requires the patient's cancer to be stable enough to delay treatment a couple of weeks. Gathering multiple eggs or embryos gives a patient the best chance of successful pregnancy later, especially for women older than 40. We can test the frozen embryos for their genetic risk for certain cancers if detected in the patient, such as the *BRCA* gene for breast cancer, but this can limit the number of embryos available for implantation.

Another potential fertility preservation method is injection with a medicine called gonadotropin-releasing hormone (GnRH) agonist. This drug suppresses the normal function of the ovaries and can put the patient into a false menopausal state, potentially sparing the egg-producing tissue from damage during chemotherapy. A series of studies found that receiving a GnRH agonist before chemotherapy for breast cancer increased women's chances of becoming pregnant after treatment. However, other studies have been inconclusive. This option is only partially protective, and some patients might not benefit.

*Cryopreservation of Ovarian Tissue* - a treatment called ovarian tissue freezing might be an option. During this procedure, strips of tissue from the ovaries are removed and frozen. This tissue contains many viable eggs that can be spared from damage during the freezing and thawing process. Once the patient has completed treatment and reaches the age at which she wants to start a family, she can have her frozen ovary tissue transplanted back to attempt to conceive naturally or through IVF. Small studies of this treatment are encouraging, but more research is needed.

### **How to Preserve Fertility when Diagnosed with Cancer**

- If possible, carefully select the chemotherapeutic agents in consultation with one's treating doctor. By doing this, women (and men) may help decrease the incidence of infertility because of cancer treatment.
- Infertility caused by cancer treatments is influenced by age. Women in their 30's are capable of tolerating much higher doses of chemotherapy drugs than women in their 40's or older, without experiencing menopause, either temporarily or permanently.

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- Where pelvic radiation therapy is indicated for cancer treatment, treating physicians should consider relocation of the ovaries (oophoropexy).
- Chemotherapy can cause damage or failure of the ovaries. The ovaries are essential to a woman's ability to become pregnant. Women in their 40's are closer to menopause, and experience symptoms of menopause and infertility more frequently because of chemotherapy damage to their ovaries.
- Hormones may help alleviate some of the menopausal symptoms but may not be recommended for oestrogen positive breast cancer patients, or those patients with hormone sensitive tumours.
- The chemotherapy agents most associated with these symptoms are the alkylating agents (listed above) and should be utilised with care.
- For women, the ability to retrieve eggs and storing ova (eggs), can be done at some centres. Unfortunately, freezing unfertilized eggs has as yet not been successful, and is not available at many centres, however, freezing embryos (fertilized eggs) has resulted in pregnancy.
- Major centres are continually involved in research to preserve female fertility and centres where success in reducing infertility, should be centres of choice. As previously mentioned, this is unfortunately not necessarily available to women accessing cancer treatment in the public sector in South Africa.

### Questions to Ask One's Health Care Team

Consider asking the following questions:

- Will my cancer treatment plan affect my ability to have children?
- Are there ways to preserve my fertility before I start treatment?
- Will my treatment plan cause problems during pregnancy, labour, or delivery?
- How long should I wait before trying to have a child?
- How will trying to have a child affect my follow-up care plan?
- Will trying to have a child increase my risk of recurrence of cancer?
- Should I talk with an obstetrician who has experience with cancer survivors?
- Where can I find emotional support for myself? For my spouse or partner?

### Men, Partners, and Others

Men can usually try to have a child soon after cancer treatment ends.

There does not appear to be firm rules for how long men should wait after treatment, but health care providers usually recommend waiting 2 to 5 years. Sperm may be damaged by chemotherapy or radiation therapy. Those sperm should be replaced in 2 years. Even if a child is conceived soon after treatment ends, there is no current research showing that he or she will have a greater risk of developing serious health problems.

*Fertility treatments for men and boys with cancer* - Sperm banking, or freezing sperm, is a well-established preservation method for men of reproductive age before they begin cancer treatment.

A male infertility expert can help to obtain sperm that could not be collected naturally. For boys and young men in their early teens or who cannot collect, harvesting sperm can be an issue. One approach that can be used is called electroejaculation, in which the patient is given a general anaesthesia and a safe electrical probe is used to help produce semen for collection. In some cases, a male infertility expert also can perform surgery to retrieve sperm directly from the testicles for freezing.

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### Cryopreservation of Ovarian Tissue

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### Drugs that May Increase Risk of Infertility in Females

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### **Embryo Transfer**

<https://advancedfertility.com/ivf-in-detail/embryo-transfer/>

### **Fathering a Child After Cancer Treatment**

<https://www.cancer.net/survivorship/life-after-cancer/having-baby-after-cancer-pregnancy>

### **Fertility Options**

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### **Having a Baby After Cancer**

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<https://www.cancer.org/cancer/breast-cancer/living-as-a-breast-cancer-survivor/pregnancy-after-breast-cancer.html>

### **Hormonal Contraceptives and Breast Cancer**

<https://www.breastcancer.org/research-news/do-hormonal-contraceptives-increase-risk>

### **Hormone Therapy**

<https://www.cancervic.org.au/living-with-cancer/common-side-effects/fertility/women-s-fertility-and-cancer-treatment.html>

### **Immunotherapy**

<https://www.cancervic.org.au/living-with-cancer/common-side-effects/fertility/women-s-fertility-and-cancer-treatment.html>

### **In Vitro Maturation**

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