
CANCER FACTS

National Cancer Institute • National Institutes of Health
Department of Health and Human Services

Oral Contraceptives and Cancer Risk

Key Points

- There is evidence of an increased risk of breast cancer for women under age 35 who are recent users of OCs (see section on Breast Cancer).
- Studies have consistently shown that using OCs reduces the risk of ovarian cancer (see section on Ovarian and Endometrial Cancers).
- There is evidence that long-term use of OCs may increase the risk of cancer of the cervix (see section on Cancer of the Cervix).
- There is some evidence that OCs may increase the risk of certain cancerous liver tumors (see section on Liver Tumors).
- References

Introduction

Oral contraceptives (OCs) first became available to American women in the early 1960s. The convenience, effectiveness, and reversibility of action of birth control pills (popularly known as “the pill”) have made them the most popular form of birth control in the United States. However, concerns have been raised about the role that hormones might play in a number of cancers, and how hormone-based OCs contribute to their development.

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This fact sheet addresses only what is known about OC use and the risk of developing cancer. It does not deal with the role of menopausal hormone use or the most serious side effect of OC use—the increased risk of cardiovascular disease for certain groups of women.

Oral Contraceptives

Currently, two types of OCs are available in the United States. The most commonly prescribed OC contains two man-made versions of natural female hormones (estrogen and progesterone) that are similar to the hormones the ovaries normally produce. Estrogen stimulates the growth and development of the uterus at puberty, causes the endometrium (the inner lining of the uterus) to thicken during the first half of the menstrual cycle, and influences breast tissue throughout life, but particularly from puberty to menopause.

Progesterone, which is produced during the last half of the menstrual cycle, prepares the endometrium to receive the egg. If the egg is fertilized, progesterone secretion continues, preventing release of additional eggs from the ovaries. For this reason, progesterone is called the “pregnancy-supporting” hormone, and scientists believe that it has valuable contraceptive effects. The man-made progesterone used in OCs is called progestogen or progestin.

The second type of OC available in the United States is called the minipill. It contains only a progestogen. The minipill is less effective in preventing pregnancy than the combination pill, so it is prescribed less often.

Because medical research suggests that cancers of the female reproductive organs depend on naturally occurring sex hormones for their development and growth, scientists have been investigating a possible link between OC use and cancer risk. Researchers have focused a great deal of attention on OC users over the past 40 years. This scrutiny has produced a wealth of data

on OC use and the development of certain cancers, although results of these studies have not always been consistent.

Breast Cancer

A woman's risk of developing breast cancer depends on several factors, some of which are related to her natural hormones. Hormonal factors that increase the risk of breast cancer include conditions that may allow high levels of hormones to persist for long periods of time, such as early age at first menstruation (before age 12), late age at menopause (after age 55), having children after age 30, and not having children at all.

Because many of the risk factors for breast cancer are related to natural hormones, and because OCs work by manipulating these hormones, there has been some concern about the possible effects of medicines such as OCs on breast cancer risk, especially if women take them for many years. Sufficient time has elapsed since the introduction of OCs to allow investigators to study large numbers of women who took birth control pills for many years. Even so, the results of some of these studies have not been consistent.

In an NCI-sponsored study published in 2003, researchers examined risk factors for breast cancer among women ages 20 to 34 compared with women ages 35 to 54. Researchers analyzed data from 2,202 women who were diagnosed with breast cancer between 1990 and 1992, and 2,209 women who did not have breast cancer. The results indicated that the risk of breast cancer was significantly increased for women ages 20 to 34 who had used OCs for at least 6 months. The risk associated with OC use was strongest for women who had used OCs within 5 years of breast cancer diagnosis. Although also elevated, the risk was weaker for women over age 35 and those who used OCs for longer periods of time.

A 1996 analysis of worldwide epidemiologic data conducted by the Collaborative Group on Hormonal Factors in Breast Cancer found that women who were current or recent users of birth control pills had a slightly elevated risk of developing breast cancer. However, 10 years or more after they stopped using OCs, their risk of developing breast cancer returned to the same level as if they had never used birth control pills. In addition, breast cancers diagnosed in women after 10 or more years of not using OCs were less advanced than breast cancers diagnosed in women who had never used OCs. To conduct this analysis, the researchers examined the results of 54 studies. The analysis involved 53,297 women with breast cancer and 100,239 women without breast cancer. More than 200 researchers participated in this combined analysis of their original studies, which represented about 90 percent of the epidemiological studies throughout the world that had investigated the possible relationship between OCs and breast cancer.

The return of risk to normal levels after 10 years or more of not taking OCs was consistent regardless of family history of breast cancer, reproductive history, geographic area of residence, ethnic background, differences in study design, dose and type of hormone, and duration of use. The change in risk also generally held true for age at first use; however, for reasons that were not fully understood, there was a continued elevated risk among women who had started to use OCs before age 20.

The findings of the Women's Contraceptive and Reproductive Experience (Women's CARE) study were in contrast to those described above. The Women's CARE study examined the use of OCs as a risk factor for breast cancer in women ages 35 to 64. Researchers interviewed 4,575 women who were diagnosed with breast cancer between 1994 and 1998, and 4,682 women who did not have breast cancer. Investigators collected detailed information about

the participants' use of OCs, reproductive history, health, and family history. The results, which were published in 2002, indicated that current or former use of OCs among women ages 35 to 64 did not significantly increase the risk of breast cancer. The findings were similar for white and black women. Factors such as longer periods of use, higher doses of estrogen, initiation of OC use before age 20, and OC use by women with a family history of breast cancer were not associated with an increased risk of the disease.

Ovarian and Endometrial Cancers

Studies have consistently shown that using OCs reduces the risk of ovarian cancer. In a 1992 analysis of 20 studies of OC use and ovarian cancer, researchers from Harvard Medical School found that the risk of ovarian cancer decreased with increasing duration of OC use. Results showed a 10- to 12-percent decrease in risk after 1 year of use, and approximately a 50-percent decrease after 5 years of use. This association between OC use and decreased risk of ovarian cancer has also been observed among women who have certain genetic changes in the BRCA1 or BRCA2 gene that increase their risk of ovarian cancer.

The results of the Cancer and Steroid Hormone Study (CASH), which was conducted by the Centers for Disease Control and Prevention and published in 1987, indicated that the longer a woman had used OCs, the lower her risk of ovarian cancer. The decrease in risk persisted long after OC use stopped. The risk-reducing effect of OCs appeared in both older and younger women, and in women with and without children. Several hypotheses have been offered to explain how oral contraceptives might protect against ovarian cancer, such as a reduction in the number of ovulations a woman has during her lifetime, but the exact mechanism is still not known.

Researchers have also found that OC users have a reduced risk of endometrial cancer. Findings from the CASH study and other reports show that combination OC use can protect against the development of endometrial cancer. The level of risk reduction is greater in women who have used OCs for a longer time, and the protection apparently persists after women have stopped taking OCs.

The reduction in risk of ovarian and endometrial cancers from OC use does not apply to the sequential type of pill, in which each monthly cycle contains 16 estrogen pills followed by 5 estrogen-plus-progesterone pills. (Sequential OCs were taken off the market in 1976, so few women have been exposed to them.) Researchers believe OCs reduce ovarian and endometrial cancer risk only when the estrogen content of birth control pills is balanced by progestogen in the same pill.

Cancer of the Cervix

There is evidence that long-term use of OCs (10 or more years) may be associated with an increased risk of cancer of the cervix (the narrow, lower portion of the uterus). A 2003 analysis by the International Agency for Research on Cancer found an increased risk of cervical cancer with longer use of OCs. Researchers analyzed data from 28 studies that included 12,531 women with cervical cancer. The data suggested that the risk of cervical cancer may decrease after OC use stops. However, more research is needed to determine the extent to which women remain at risk for cervical cancer after they stop using OCs.

Human Papillomavirus (HPV)

Of the more than 100 types of human papillomavirus (HPV), over 30 types can be passed from one person to another through sexual contact. HPVs are some of the most common sexually transmitted infections. Approximately 15 HPVs are known to cause cervical cancer. Compared to non-OC users, women who use OCs may be less likely to use barrier methods of contraception (such as condoms). Because condoms are partially effective in preventing HPV infection, OC users who do not use condoms may be at increased risk of becoming infected with HPV. Therefore, the increased risk of cervical cancer that some studies found to be caused by prolonged OC use may actually be the result of HPV infection.

Researchers are studying whether other factors such as multiple births and the use of OCs work together with sexually transmitted agents (such as HPVs) in the development of cervical cancer. Findings from an analysis of 10 studies suggested that long-term use of OCs may increase the risk of cervical cancer by up to 4 times in women who are infected with HPV.

However, in another long-term study published in 2002, researchers concluded that OC use did not increase the risk of cervical cancer in a well-screened population. The researchers followed a group of HPV-diagnosed women for 10 years. The participants were asked questions about OC use (but not the duration of use), smoking, and number of children. The results showed that HPV-diagnosed women who used OCs did not have a higher risk of cervical cancer than women who did not use OCs.

More research is needed into the exact nature of the association between OC use and risk of cervical cancer. One reason the association is unclear is that the major risk factor for cervical cancer (history of genital HPV infection) is related to sexual behavior. Because sexual behavior may be different between women who use OCs and those who have never used them, it is

difficult for researchers to determine the exact role that OCs may play in the development of cervical cancer.

Liver Tumors

There is some evidence that OCs may increase the risk of certain malignant (cancerous) liver tumors. However, the risk is difficult to evaluate because of different patterns of OC use and because these tumors are rare in American women (the incidence is approximately 2 cases per 100,000 women). A benign (noncancerous) tumor of the liver called hepatic adenoma has also been found to occur, although rarely, among OC users. These tumors do not spread, but they may rupture and cause internal bleeding.

Reducing Risks Through Screening

Studies have found that breast cancer screening with mammograms reduces the number of deaths from breast cancer for women ages 40 to 69. Women who are at increased risk for breast cancer should seek medical advice about when to begin having mammograms and how often to be screened. A high-quality mammogram, with a clinical breast exam (an exam done by a professional health care provider), is the most effective way to detect breast cancer early.

Abnormal changes in the cervix can often be detected by a Pap test and treated before cancer develops. Women who have begun to have sexual intercourse or are age 21 should check with their doctor about having a Pap test.

Women who are concerned about their risk for cancer are encouraged to talk with their health care provider. More information is also available from the Cancer Information Service (see below).

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1–800–4–CANCER (1–800–422–6237)

TTY (for deaf and hard of hearing callers): 1–800–332–8615

NCI Online

Internet

Use <http://cancer.gov> to reach the NCI's Web site.

LiveHelp

Cancer Information Specialists offer online assistance through the *LiveHelp* link on the NCI's Web site.

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