

Oral Contraceptives and Cancer Risk

What are oral contraceptives?

Oral contraceptives (birth control pills) are hormone-containing medications that are taken by mouth to prevent pregnancy. They prevent pregnancy by inhibiting ovulation and also by preventing sperm from penetrating through the cervix.

By far the most commonly prescribed type of oral contraceptive in the United States contains synthetic versions of the natural female hormones estrogen and progesterone. This type of birth control pill is often called a combined oral contraceptive. Another type of oral contraceptive, sometimes called the mini pill, contains only progestin, which is a man-made version of progesterone.

What is known about the relationship between oral contraceptive use and cancer?

Nearly all the research on the link between oral contraceptives and cancer risk comes from observational studies, both large prospective cohort studies and population-based case-control studies. Data from observational studies cannot definitively establish that an exposure—in this case, oral contraceptives—causes (or prevents) cancer. That is because women who take oral contraceptives may differ from those who don't take them in ways other than their oral contraceptive use, and it is possible that these other differences—rather than oral contraceptive use—are what explains their different cancer risk.

Overall, however, these studies have provided consistent evidence that the risks of breast and cervical cancers are increased in women who use oral contraceptives, whereas the risks of endometrial, ovarian, and colorectal cancers are reduced (1–3).

- **Breast cancer:** An analysis of data from more than 150,000 women who participated in 54 epidemiologic studies showed that, overall, women who had ever used oral contraceptives had a slight (7%) increase in the relative risk of breast cancer compared with women who had never used oral contraceptives. Women who were currently using oral contraceptives had a 24% increase in risk that did not increase with the duration of use. Risk declined after use of oral contraceptives stopped, and no risk increase was evident by 10 years after use had stopped (4).

A 2010 analysis of data from the Nurses' Health Study, which has been following more than 116,000 female nurses who were 24 to 43 years old when they enrolled in the study in 1989, also found that participants who used oral contraceptives had a slight increase in breast cancer risk (5,

6). However, nearly all of the increased risk was seen among women who took a specific type of oral contraceptive, a “triphasic” pill, in which the dose of hormones is changed in three stages over the course of a woman’s monthly cycle. An elevated risk associated with specific triphasic formulations was also reported in a nested case–control study that used electronic medical records to verify oral contraceptive use (7).

In 2017, a large prospective Danish study reported breast cancer risks associated with more recent formulations of oral contraceptives (8). Overall, women who were using or had recently stopped using oral combined hormone contraceptives had a modest (about 20%) increase in the relative risk of breast cancer compared with women who had never used oral contraceptives. The risk increase varied from 0% to 60%, depending on the specific type of oral combined hormone contraceptive. The risk of breast cancer also increased the longer oral contraceptives were used.

- **Cervical cancer:** Women who have used oral contraceptives for 5 or more years have a higher risk of cervical cancer than women who have never used oral contraceptives. The longer a woman uses oral contraceptives, the greater the increase in her risk of cervical cancer. One study found a 10% increased risk for less than 5 years of use, a 60% increased risk with 5–9 years of use, and a doubling of the risk with 10 or more years of use (9). However, the risk of cervical cancer has been found to decline over time after women stop using oral contraceptives (10–12).
- **Endometrial cancer:** Women who have ever used oral contraceptives have a lower risk of endometrial cancer than women who have never used oral contraceptives. Risk is reduced by at least 30%, with a greater risk reduction the longer oral contraceptives were used (13). The protective effect persists for many years after a woman stops using oral contraceptives (12, 14, 15). An analysis of women participating in the prospective NIH-AARP Diet and Health Study found that the risk reduction was especially pronounced in long-time users of oral contraceptives who were smokers, had obesity, or exercised rarely (13).
- **Ovarian cancer:** Women who have ever used oral contraceptives have a 30% to 50% lower risk of ovarian cancer than women who have never used oral contraceptives (16–18). This protection has been found to increase with the length of time oral contraceptives are used (13) and to continue for up to 30 years after a woman stops using oral contraceptives (17). A reduction in ovarian cancer risk with use of oral contraceptives is also seen among women who carry a harmful mutation in the *BRCA1* or *BRCA2* gene (19–21).
- **Colorectal cancer:** Oral contraceptive use is associated with 15% to 20% lower risks of colorectal cancer (12, 14, 22, 23).

How could oral contraceptives influence cancer risk?

Naturally occurring estrogen and progesterone stimulate the development and growth of some cancers (e.g., cancers that express receptors for these hormones, such as breast cancer). Because

birth control pills contain synthetic versions of these female hormones, they could potentially also increase cancer risk.

In addition, oral contraceptives might increase the risk of cervical cancer by changing the susceptibility of cervical cells to persistent infection with high-risk HPV types (the cause of virtually all cervical cancers).

Researchers have proposed multiple ways that oral contraceptives may lower the risks of some cancers, including

- suppressing endometrial cell proliferation (endometrial cancer)
- reducing the number of ovulations a woman experiences in her lifetime, thereby reducing exposure to naturally occurring female hormones (ovarian cancer)
- lowering the levels of bile acids in the blood for women taking oral conjugated estrogens (colorectal cancer) (23)

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