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Q/ Do oral contraceptives put women with a family history of breast cancer at increased risk?

EVIDENCE-BASED ANSWER

A/ No. Modern combined oral contraceptive pills (OCPs) don't increase breast cancer risk in women with a family history (strength of recommendation [SOR]: **B**, systematic review of cohort, case-control studies). However, older, higher-dose OCPs (in use before 1975) did

increase breast cancer risk in these women (SOR: **C**, case-control study).

Similarly, modern OCPs don't raise breast cancer risk in women with BRCA1/2 mutations, although higher-dose, pre-1975 OCPs did (SOR: **B** and **C**, a meta-analysis of cohort and case-control studies).

Evidence summary

A systematic review of the effect of combined OCPs on women with a family history of breast cancer found no additional increase in risk.¹ Investigators identified 3 retrospective cohort studies (N=66,500, with 8500 cases) and 7 case-control studies (total 10,500 cases) from the past 40 years, most including women from the United States and Canada, but one including women from 5 continents.

In most trials, women of reproductive age using combined OCPs had 1 or more first-degree female relatives with breast cancer, although a few trials also included second-degree relatives. Women ranged in age from 20 to 79 years at diagnosis, and most trials controlled for age, parity, menstrual and menopausal history, duration of OCP exposure, and age at first use. Follow-up intervals for the retrospective cohort studies ranged from 5 to 16 years. Investigators were unable to combine results because of heterogeneous populations.

Three of the cohort studies found no significant difference in breast cancer risk between OCP users and nonusers, regardless of age or duration of use. One cohort

study found an increased risk in women taking older, higher-dose OCPs from before 1975 (relative risk [RR]=3.3; 95% confidence interval [CI], 1.5-7.2). All of the case-control studies found no significant difference in breast cancer risk for any age of starting, duration of OCP use, or degree of relative with breast cancer.

A meta-analysis of 54 case-control studies (6757 cases), comprising approximately 90% of the epidemiologic information on this topic, also found no significant difference in breast cancer risk related to OCP use among women with one or more first-degree relatives with breast cancer.² Investigators found that neither recent OCP use (<10 years, RR=0.77; 95% CI, 0.54-1.11) nor past OCP use (>10 years, RR=1.01; 95% CI, 0.80-1.28) affected risk of developing breast cancer.

Three additional case-control studies involving women with a family history of breast cancer also found no significant association for breast cancer incidence among OCP users compared with nonusers.³⁻⁵

Modern combined OCPs don't raise risk in women with BRCA1/2 mutations

A meta-analysis of 5 studies (one retrospec-

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tive cohort, 4 case-control, with a total of 2855 breast cancer cases and 2944 controls) evaluated whether combined OCPs increased the risk of breast cancer in women, all of whom were carrying BRCA1/2 mutations.⁶

Using modern combined OCPs didn't raise the risk of breast cancer in BRCA1/2 carriers overall (RR=1.13; 95% CI, 0.88-1.45) or separately in BRCA1 carriers (5 studies, RR=1.09; 95% CI, 0.77-1.54) or BRCA2 carriers (3 studies, RR=1.15; 95% CI, 0.88-1.45).

However, pre-1975 (higher dose) combined OCPs produced significantly increased risk (RR=1.47; 95% CI, 1.06-2.04). Similarly, women who had used combined OCPs >10 years before the study (older women, likely to have been using pre-1975 OCPs) also had significantly increased risk (RR=1.46; 95% CI, 1.07-2.07).

A bit of good news:

Combined OCPs reduce ovarian cancer risk

The analysis also determined that combined OCPs significantly reduced the

risk of ovarian cancer in women carrying BRCA1/2 mutations (RR=0.50; 95% CI, 0.33-0.75), with an additional linear decrease in risk for each 10 years of OCP use (RR=0.64; 95% CI, 0.53-0.78).

Recommendations

The World Health Organization guidelines outlining criteria for contraceptive use state that OCPs don't alter the risk of breast cancer among women with either a family history of breast cancer or breast cancer susceptibility genes.⁷

The American College of Obstetricians and Gynecologists (ACOG) says that a positive family history of breast cancer shouldn't be regarded as a contraindication to OCP use.⁸ ACOG also says that women with the BRCA1 mutation have an increased risk of breast cancer if they used OCPs for longer than 5 years before age 30, but this risk may be more than balanced by the benefit of a greatly reduced risk of ovarian cancer. **JFP**



Combined oral contraceptive pills significantly reduced the risk of ovarian cancer in women carrying BRCA1/2 mutations.

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