

How does oral contraceptive use affect one's risk of ovarian, endometrial, breast, and colorectal cancers?

Oral contraceptives (OCs) are associated with a decreased risk of ovarian and endometrial cancers across multiple modifiable lifestyle characteristics. There may be an **increased risk of breast cancer** with OC use.

Michels KA, Pfeiffer RM, Brinton LA, Trabert B. Modification of the associations between duration of oral contraceptive use and ovarian, endometrial, breast, and colorectal cancers [published online January 18, 2018]. JAMA Oncol. doi:10.1001/jamaoncol.2017.4942.

may be altered by other modifiable lifestyle characteristics, such as smoking, alcohol use, obesity, and physical activity.

Details of the study

Michels and colleagues evaluated the association between OC use and multiple cancers, stratifying these risks by duration of use and various modifiable lifestyle characteristics.³ The authors used a prospective survey-based cohort (the NIH-AARP Diet and Health Study) linked with state cancer registries to evaluate this relationship in a diverse population of 196,536 women across 6 US states and 2 metropolitan areas. Women were enrolled in 1995–1996 and followed until 2011. Cancer risks were presented as hazard ratios (HR), which indicate the risk of developing a specific cancer type in OC users compared with nonusers. HRs differ from relative risks (RR) and odds ratios because they compare the instantaneous risk difference between the 2 groups, rather than the cumulative risk difference over the entire study period.⁴

Duration of OC use and risk reduction

In this study population, OC use was associated with a significantly decreased risk of ovarian cancer, and this risk increased with longer duration of use (TABLE). Similarly, long-term OC use was associated with a decreased risk for endometrial cancer. These

EXPERT COMMENTARY

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Hormonal contraception (HC), including OC, is a central component of women's health care worldwide. In addition to its many potential health benefits (pregnancy prevention, menstrual symptom management), HC use modifies the risk of various cancers. As we discussed in the February 2018 issue of OBG MANAGEMENT, a recent large population-based study in Denmark showed a small but statistically significant increase in breast cancer risk in HC users.^{1,2} Conversely, HC use has a long recognized protective effect against ovarian and endometrial cancers. These risk relationships

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FAST TRACK

OC use was associated with a significantly decreased risk of ovarian cancer and a decreased risk of endometrial cancer—regardless of smoking status, alcohol use, BMI, and physical activity

TABLE Risks of developing any cancer with OC use

Hazard ratio (95% confidence interval) for cancers by duration of OC use ³				
Type of cancer	Incidence in US women ^a	1–4 years of OC use	5–9 years of OC use	10+ years of OC use
Ovarian	11.7 ¹⁷	0.82 (0.69–0.97)	0.72 (0.59–0.88)	0.60 (0.47–0.76)
Endometrial	25.7 ¹⁸	0.79 (0.70–0.90)	0.84 (0.73–0.97)	0.66 (0.56–0.78)
Breast	124.9 ¹⁹	1.04 (0.98–1.10)	1.02 (0.96–1.09)	1.04 (0.97–1.11)
Colorectal	35.1 ²⁰	0.94 (0.85–1.05)	0.97 (0.86–1.10)	1.03 (0.91–1.18)

Abbreviation: OC, oral contraceptives.

^aPer 100,000 women per year. These rates are age adjusted and are based on 2010–2014 data from the Surveillance, Epidemiology, and End Results Program.

effects were true across various lifestyle characteristics, including smoking status, alcohol use, body mass index (BMI), and physical activity level.

There was a nonsignificant trend toward increased risk of breast cancer among OC users. The most significant elevation in breast cancer risk was found in long-term users who were current smokers (HR, 1.21 [95% confidence interval (CI), 1.01–1.44]).

OC use had a minimal effect on colorectal cancer risk.

The bottom line. US women using OCs were significantly less likely to develop ovarian and endometrial cancers compared with nonusers. This risk reduction increased with longer duration of OC use and was true regardless of lifestyle. Conversely, there was a trend toward a slightly increased risk of developing breast cancer in OC users.

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WHAT THIS EVIDENCE MEANS FOR PRACTICE

According to the study by Michels and colleagues, overall, women using OCs had a decreased risk of ovarian and endometrial cancers and a trend toward a slightly increased risk of breast cancer.³ Based on this and prior estimates, the overall risk of developing any cancer appears to be lower in OC users than in nonusers.^{5,6}

Consider discussing the points below when counseling women on OC use and cancer risk.

Cancer prevention

- OC use was associated with a significantly decreased risk of both ovarian and endometrial cancers. This effect increased with longer duration of use.
- Ovarian cancer risk reduction persisted regardless of smoking status, BMI, alcohol use, or physical activity level.
- The largest reduction in endometrial cancer was seen in current smokers and patients with a BMI greater than 30 kg/m².

Breast cancer risk

- There was a trend toward a slightly increased risk of breast cancer with OC use of any duration.
- A Danish cohort study showed a significantly higher risk (although still an overall low risk) of breast cancer with HC use (RR, 1.20 [95% CI, 1.14–1.26]).¹
- The differences in these 2 results may be related to study design and population characteristic differences.

Overall cancer risk

- The definitive and larger risk reductions in ovarian and endometrial cancer compared with the lesser risk increase in breast cancer suggest a *net decrease* in developing any cancer for OC users.^{3,5,6}

Risks of pregnancy prevention failure

- OCs are an effective method for preventing unintended pregnancy. Risks of OCs should be weighed against the risks of unintended pregnancy.
- In the United States, the maternal mortality rate (2015) is 26.4 deaths for every 100,000 women.⁷ The risk of maternal mortality is substantially higher than even the highest published estimates of HC-attributable breast cancer rates (that is, 13 incremental breast cancers for every 100,000 women using HC; 2 incremental breast cancers for every 100,000 women 35 years of age or younger using HC).¹
- Unintended pregnancy is a serious maternal-child health problem, and it has substantial health, social, and economic consequences.^{8–14}
- Unintended pregnancies generate a significant economic burden (an estimated \$21 billion in direct and indirect costs for the US health care system per year).¹⁵ Approximately 42% of unintended pregnancies end in abortion.¹⁶

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Study strengths and weaknesses

The effect on breast cancer risk is less pronounced than that reported in a recent large, prospective cohort study in Denmark, which reported an RR of developing breast cancer of 1.20 (95% CI, 1.14–1.26) among all current or recent HC users.¹ These differing results may be due to the US study population's increased heterogeneity compared with the Danish cohort; potential recall bias in the US study (not present in the Danish study

because pharmacy records were used); the larger size of the Danish study (that is, ability to detect very small effect sizes); and lack of information on OC formulation, recency of use, and parity in the US study.

Nevertheless, the significant protective effect against ovarian and endometrial cancers (reported previously in numerous studies) should be a part of totality of cancer risk when counseling patients on any potential increased risk of breast cancer with OC use. ●

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When counseling patients on any potential risk of breast cancer with OC use, also discuss OCs' significant protective effect against ovarian and endometrial cancers