FSRH CEU Statement: Response to study

Contemporary Hormonal Contraception and the Risk of Breast Cancer

12th December 2017

An observational study1 published in the New England Journal of Medicine reports that, in the Danish study population, women who were currently using any method of hormonal contraception* (HC) or had done so within the last 6 months were 20% more likely to be diagnosed with breast cancer than those who had never used HC. Young women are at low risk of breast cancer and a 20% increase represents a small number of cases; in the study population, approximately one extra breast cancer was diagnosed for every 7,690 women aged 15 to 49 years using hormonal contraception for 1 year. The risk reduced with time after stopping HC.

About the study

- The study included the 1.8 million Danish women aged 15-49 years between 1995 and 2012. Women who had had cancer, VTE or fertility treatment were excluded.
- Information regarding use of HC*, breast cancer diagnoses and potential confounding factors was obtained from national databases. 24% of Danish women used HC in 1995, increasing to 39% in 2012.
- During 19.6 million woman-years of follow up, 11,517 breast cancers were diagnosed.
- Results were adjusted for factors including age, PCOS, parity and family history of breast or ovarian cancer. However, information relating to potential confounding factors such as age at menarche, breastfeeding and alcohol consumption was not available and BMI data were incomplete.

Key findings

- Current and recent users of (any) HC were at 20% increased risk of developing breast cancer compared to never users of hormonal contraceptives (adjusted relative risk (RR)1.20 [95% confidence interval 1.14-1.26]).

- The absolute increase in breast cancers diagnosed among current and recent HC users was small. Among women aged 15-49 who had never used HC, 55 incident breast cancers were observed per 100,000 woman-years. Among current or recent HC users, 13 additional breast cancers (95% CI, 10 to 16) were observed per 100,000 woman-years - approximately 1 extra breast cancer for every 7,690 women using HC for 1 year.

Type of hormonal contraceptive

- The relative risk of breast cancer associated with current or recent use of combined oral contraceptives (COC) compared to never-use of HC varied between 1.0 and 1.6, depending on formulation. Meaningful differences in risk between COC preparations were not identified.
Women who currently or recently used the levonorgestrel-releasing IUS (LNG-IUS) also had a significantly higher risk of breast cancer than women who had never used hormonal contraceptives (relative risk, 1.21; 95% CI, 1.11 to 1.33).

Numbers of users of non-oral combined hormonal contraception and other progestogen-only methods in the study were much smaller than the numbers of users of COC and the LNG-IUS. For these methods a significant increase in breast cancer risk compared to never-users of HC was observed only with use of the levonorgestrel progestogen-only pill (adjusted RR 1.93; 95% CI 1.18-3.16), for which only 10,547 women-years of exposure and 16 incident breast cancers were observed.

Duration of use of HC and risk after discontinuation

Breast cancer risk increased with longer duration of HC use. Compared to women who had never used HC, the risk of breast cancer with current or recent use of HC increased from 1.09 (95% CI, 0.96 to 1.23) with less than 1 year of use to 1.38 (95% CI, 1.26 to 1.51) with more than 10 years of use (P = 0.002).

No increased risk was found among women who had previously used HC for less than 5 years.

Among women who had used HC for 5 years or more, the risk of breast cancer was still higher after discontinuation than that for women who had never used HC.

The study does not consider the effect of HC use on risk of breast cancer recurrence.

What does the study add to what we already know?

In line with the findings of this study, previous large observational studies have identified an increased breast cancer risk in current and recent COC users which disappears over time. A collaborative reanalysis of data from 54 epidemiological studies reporting on 53,297 women with breast cancer and 100,239 women without breast cancer found a relative risk for breast cancer of 1.24 [1.15-1.33] amongst current COC users. The risk reduced with time after stopping and was not significant by 10 years after discontinuation.² The Royal College of General Practitioners’ (RCGP) Oral Contraception Study³ examined the long-term cancer effects associated with oral contraception by following an original cohort of 46,000 women for up to 44 years. The study found an increased risk of breast and cervical cancer in current and recent pill users, which disappeared within approximately 5 years of stopping oral contraception.

Existing data relating to breast cancer risk associated with use of progestogen-only contraceptives are limited. The collaborative reanalysis above included very few users of progestogen-only contraceptive methods, but suggested findings broadly similar to those for COC.² A case control study⁴ observed no increase in breast cancer risk associated with use of the LNG-IUS compared to Cu-IUD use, but was powered only to detect a 1.5-fold increased risk. Data from a large post-marketing study identified no significant difference between breast cancer risk associated with use
of the LNG-IUS than for the general Finnish population.5

**Implications for clinical practice**
The findings of this study do not alter existing FSRH advice to UK prescribers. Women should be informed of the small apparent increase in breast cancer risk associated with current or recent use of HC. They should be advised that risk reduces with time after stopping HC. This risk must be weighed against the benefit of effective contraception and non-contraceptive benefits including management of heavy menstrual bleeding and menstruation-related symptoms. Combined oral contraception has the additional significant benefit of long-lasting reduced risk of ovarian, endometrial, and perhaps colorectal cancer.3 Details of the benefits and risks associated with contraceptive methods can found in FSRH Clinical Guidelines, available on the FSRH website.5-7[ref]

*Hormonal contraceptives considered included combined oral contraceptives, combined patch and vaginal ring, progestogen-only pills, progestogen-only subdermal implant, depot medroxyprogesterone acetate (DMPA) and levonorgestrel-releasing intrauterine system (LNG-IUS).

**References**
The Clinical Effectiveness Unit (CEU) was formed to support the Clinical Effectiveness Committee of the Faculty of Sexual and Reproductive Healthcare (FSRH), the largest UK professional membership organisation working at the heart of sexual and reproductive healthcare. The FSRH CEU promotes evidence based clinical practice and it is fully funded by the FSRH through membership fees. It is based in Edinburgh and it provides a member’s enquiry service, evidence based guidance, new SRH product reviews and clinical audit/research. Find out more here.