Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies

Collaborative Group on Hormonal Factors in Breast Cancer

**Authors' objectives**

To assess the epidemiological evidence on the relationship between breast cancer risk and the use of oral contraception.

**Searching**

The studies were identified from review articles, from a computer-aided literature search, discussions with colleagues, and from discussion with the principal investigator of all identified studies. Both published and unpublished articles were considered for review.

**Study selection**

Study designs of evaluations included in the review

Prospective studies and case-control studies with at least 100 women with breast cancer, which included information on the use of oral contraceptives and reproductive history.

Specific interventions included in the review

Oral contraceptive use: combined oral contraception (COC) containing varying doses of oestrogen and progesterone. Preparations containing low, medium and high (less than 50, 50, and greater than 50 microg, respectively) doses of oestrogen.

Participants included in the review

The studies included 53,279 women with breast cancer and 100,239 controls from 25 countries.

Outcomes assessed in the review

Breast cancer (localised or spread beyond the breast) was assessed.

**How were decisions on the relevance of primary studies made?**

The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

**Assessment of study quality**

The authors do not state that they assessed quality.

**Data extraction**

The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction. Data extracted included sociodemographic information, use of hormonal contraceptives and hormone replacement, reproductive history, family history of breast cancer, age of menarche, height, weight, menopausal status, age at menopause, gynaecological history and alcohol consumption.

**Methods of synthesis**

How were the studies combined?

The studies were combined using the Mantel-Haenszel stratification technique where all analyses were stratified by study and other factors. Stratum-specific quantities calculated are standard observed minus expected numbers of women with breast cancer. The relative risk (RR) was obtained by a one-step method. Factors used for stratification
were study, centre, reproductive history, age of menopause, age of first birth. Women with unknown values for a particular stratification were allocated to a separate stratum.

How were differences between studies investigated?
Heterogeneity of RR was assessed using chi-squared tests. Chi-squared tests between studies, and between study designs, were performed for each set of RRs calculated.

Results of the review
Ten prospective studies, 25 case-control studies with population control, and 14 case-control studies with hospital controls were included (52,925 cases and 99,018 controls).

For women currently taking COC, and for 10 years after stopping, there was a small increase in the RR of breast cancer.

Current users, RR 1.24 (95% confidence interval, CI: 1.15, 1.33, 2p>0.00001); 1 to 4 years after stopping COC, RR 1.16 (95% CI: 1.08, 1.23, 2p=0.00001); 5 to 9 years after stopping COC, RR 1.07 (95% CI: 1.02, 1.13, 2p=0.009).

There was no significant excess risk of having breast cancer diagnosed 10 or more years after stopping COC: RR 1.0 (95% CI: 0.96, 1.05, non significant). The cancers diagnosed in women who had used COC were less advanced clinically than those diagnosed in never-users. The RR of tumours that had spread beyond the breast compared to localised tumours, in ever-users compared to never-users, was 0.88 (95% CI: 0.81, 0.95, 2p=0.002).

Authors' conclusions
There is a small increase in the risk of having breast cancer diagnosed while taking oral contraception and for the 10 years after stopping. Ten years or more after stopping hormonal contraception there is little or no increase in the risk of having breast cancer diagnosed, and cancers diagnosed are less advanced clinically than the cancers diagnosed in women who have never used oral contraception.

CRD commentary
Insufficient details were given of the databases searched, but wide consultation among investigators in the field should have identified most studies. An evaluation of the quality of the primary studies would have been welcome, in particular details of the selection of the breast-cancer patients, selection of controls, and methods of data collection; the authors state that details of the design of each study and of the women included are given in another article (see Other Publications of Related Interest). Recall bias may have affected the data collected on contraceptive use. The results of the many statistical analyses were presented clearly and graphically. As the authors state, there is as yet little information beyond 20 years after cessation of use. Potential problems with the data and sources of bias were discussed by the authors, but changing patterns of contraceptive use, the use of lower oestrogen dose regimens, and any alteration in the incidence of breast cancer may produce different results in future cohort studies.

Bibliographic details

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Other publications of related interest
Indexing Status
Subject indexing assigned by NLM

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