

## Selected Summaries

### Contemporary hormonal contraceptives and breast cancer risk: What do we learn?

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#### SUMMARY

This nationwide, large prospective study conducted in Denmark included all women between 15 and 49 years of age to assess whether there was an association of modern-day hormonal contraceptives and risk of breast cancer. About 1.8 million women were followed for 10.9 years. Nationwide registries in Denmark provided individually updated information on hormonal contraception, breast cancer diagnoses and potential confounders. The study documented 11 517 cases of breast cancer in this population during the study period. The important findings of the study were:

- There was a 20% higher risk of breast cancer among women who are current or latest users of hormonal contraception.
- The risk increased with duration of use of hormonal contraception from 9% in women who used it for 1 year to 38% in women who used it for more than 10 years.
- All hormonal contraception methods including progesterone-only intrauterine device (IUD) showed an increased risk when compared with never users.
- The risk persisted even after stopping hormonal contraception in patients who had used it for more than 5 years.

The absolute increase in breast cancer among the current and the latest hormonal contraceptive users was 13/100 000 person-years or one extra breast cancer for every 7690 hormonal contraceptive users in 1 year. The authors concluded that hormonal contraceptives are associated with an increased risk of breast cancer and the risk increased with duration of use, but the absolute increase in risk is small.

#### COMMENT

Hormonal contraception (pills, hormonal IUD and injections) is a reliable form of contraception with fewer failure rates. Cancer risk remains a concern with the long-term use of hormonal contraception. To answer this, a large cohort study reported a significantly lower rate of the large bowel, uterine body and ovarian cancers, and increasing risk towards cervical and central nervous system tumours among long-term hormonal contraceptive users. The incidence of breast cancer was similar in pill users and never users in that study.<sup>1</sup> Available data on the risk of hormonal contraceptives on breast cancer are conflicting and are limited predominantly to combined oral contraceptive pills.<sup>2,3</sup> A meta-analysis of cohort studies involving 11 722 cases and over 850 000 women reported a non-significant increase in breast cancer in ever users of oral contraceptives compared with non-users (relative risk 1.08, CI 0.99–1.17).<sup>2</sup> A study from Thailand showed that oral

contraceptives might increase the risk of breast cancer.<sup>3</sup> There are no data on modern-day hormonal contraception which were considered safer options as regards to risk of breast cancer. The present study was done to ascertain if current hormonal formulations increased the risk of breast cancer.

#### What are the messages from the study?

This study is important as it adds data on current hormonal contraceptives including low-oestrogen pills, progesterone-only pills and their risk of breast cancer for which evidence was lacking; and one can conclude that no present-day formulation of hormonal contraception is free from the risk of breast cancer.

The persistent risk in women who use hormonal contraception for more than 5 years is an additional input to the existing data.

The study emphasizes how a large informative study is possible at relatively low cost to address common but important questions when nationwide registries for medicines and cancer are available and are linked with each other.

#### Critical review

Among the limitations of the study is that factors such as age at menarche, breastfeeding, alcohol consumption or physical activity, environmental and dietary aspects were not adjusted. The absolute risk of breast cancer will be determined by the woman's individual baseline risk, which includes the above factors. The authors explained that decreased occurrence of breast cancer in patients who stopped hormonal contraception within 5 years is not expected if these risk factors acted as confounders. Whether these factors influence risk in long-term users is unknown. Marsden reported that excess risk associated with hormonal contraceptives is small and comparable with the risk by other modifiable risk factors such as smoking, alcohol consumption and age at first birth for hormone-sensitive breast cancer in pre-menopausal women.<sup>4</sup>

Although there is an increased risk of breast cancer, there is no evidence that contraceptive use leads to increased breast cancer-specific mortality when compared with never users. Contraceptive users tend to be more health-conscious and likely to seek medical attention early when they have breast symptoms and this can lead to early diagnosis of breast cancer in this group, at least theoretically. It is not clear whether this increased risk is associated with advanced disease stage or increased disease-specific mortality in contraceptive users.

#### Implications for India

In India, the incidence of breast cancer is 25.8/100 000. The data of National Family Health Survey-4 have shown that only 53.5% of the population uses some form of contraception. Unlike Denmark where 39% of women in the reproductive age group use hormonal contraception, only 4.1% use it in India.<sup>5</sup> The population at risk of breast cancer due to oral contraception in our country is smaller when compared to the western world. The advantages of contraception such as good efficacy in avoiding unwanted pregnancy, reduced risk of certain malignancy, such as colorectal and endometrial, should also be considered before counselling the patient about contraception. The UK medical eligibility criteria recommendations are based on evidence and consensus opinion, which assists clinicians in prescribing safe and appropriate

contraception.<sup>6</sup> It recommends considering the individual absolute risk in women with high risk before advising contraception.

### Conclusion

Clinicians should use the data of this study to discuss the advantages and disadvantages of hormonal and non-hormonal contraceptive methods (condom, diaphragm and copper IUD) and help women make an informed decision on a contraceptive method that is most consistent with their lifestyle with minimal side-effects.

*Conflicts of interest.* None declared

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