

Progestogen-only contraception and breast cancer

Background

A 2023 study showed a slight increase in the risk of breast cancer in current and recent users of progestogen-only contraception. This risk was similar across all the progestogen-only methods. All increases in risk were statistically significant except for the contraceptive implant, where there were only a small number of cases.(1) The results align with prior research that has shown a possible association between the use of the 52 mg levonorgestrel IUD (Mirena) and the risk of breast cancer (2, 3). The study also reaffirmed a comparable risk for users of combined hormonal contraception, as previously established.(4, 5) Evidence regarding breast cancer mortality in progestogen-only users is currently unavailable, although users of combined hormonal contraception do not face an increased risk of breast cancer mortality.(6)

When using hormonal contraception, the relative risk of breast cancer increases by around 20-30%, which results in only a small number of additional breast cancers, particularly in young users. The background risk of breast cancer increases with age and diagnosis is extremely rare before the age of 30 years. The 2023 study estimates that if 100,000 people aged 16-20 used a hormonal method of contraception for 5 years there would be 2.8 breast cancers diagnosed during that time and 2.2. per 100,000 in non-users of the same age over the same time period. For users aged 35-39 years, the corresponding figures are 398.0 per 100,000 for users of hormonal contraception compared to 313.4 per 100,000 in non-users of the same age over 5 years. After stopping hormonal contraception, a residual increased risk of breast cancer remains but decreases with time and approaches no increased risk 5-9 years after stopping. (1)

Footnote: The Medical Advisory Committee of Family Planning Alliance Australia is comprised of senior medical educators, senior medical officers, and medical directors of the member family planning organisations. The Clinical Reference Group of the Medical Advisory Committee exists as a means to review current clinical practice and provide evidence and consensus-based recommendations for use by clinicians where clinical guidance is lacking.



The table below estimates the risk of breast cancer for all hormonal contraceptives based on the risks for oral combined and progestogen-only contraception.

Table 1: Estimated additional breast cancers over a 15-year period if a person uses a hormonal method of contraception for 5 years and then does not use hormonal contraception for the following				
10 years.				
Age when	Number of	Number of	Additional number	Number of
hormonal	cancers expected	cancers expected	of cancers	additional
contraception used	in 100,00	in 100,00users		cancers per
	nonusers			user
16-19 years	84.1	92.5	8.4	1 per 12,000
20-24 years	199.0	220.2	21.4	1 per 4500
25-29 years	504.7	565.8	61.1	1 per 1,500
30-34 years	1072.3	1210.3	138	1 per 700
35-39 years	1952.9	2218.0	265.1	1 per 400

Adapted from: "Estimated excess incidence of breast cancer per 100,000 women within England associated with five years use of any oral contraceptive, by age at first use."(1)

Breast cancer is a complex disease and several modifiable factors contribute to it including alcohol intake and obesity. (7) Consequently, any risks associated with the use of hormonal methods of contraception must be balanced against their considerable benefits.

In Australia progestogen-only methods available include the progestogen-only pill, the contraceptive injection, the implant and the intrauterine device. They have few contraindications and are safe choices for those with a past history or risk factors for deep vein thrombosis or cardiovascular disease and can be used during lactation.(8) Numerous studies indicate that the use of the 52 mg LNG IUD is associated with a decreased risk of endometrial cancer, and may also reduce the risk of both cervical and ovarian cancers. (9)

Long-acting reversible methods such as hormonal IUDs and the etonogestrel implant are not only highly effective but also liked by users. (10) Mirena is very effective for heavy menstrual bleeding and dysmenorrhoea and has beneficial effects on endometriosis and adenomyosis. (11-17).



Recommendations

Inform potential users of progestogen-only methods:

- there appears to be a slight increase in risk of breast cancer during use of progestogen-only methods
- the risk of breast cancer varies with age, with the background risk being very low for those aged under 30 years
- the excess risk related to the use of progestogen-only methods appears to decrease with time after discontinuation
- progestogen-only methods offer numerous benefits
- hormonal contraception is just one of several factors influencing breast cancer risk, and other modifiable factors should be taken into consideration.

References

- 1. Fitzpatrick D, Pirie K, Reeves G, Green J, Beral V. Combined and progestagen-only hormonal contraceptives and breast cancer risk: A UK nested case-control study and meta-analysis. PLoS Med. 2023;20(3):e1004188.
- 2. Conz L, Mota BS, Bahamondes L, Teixeira Doria M, Francoise Mauricette Derchain S, Rieira R, Sarian LO. Levonorgestrel-releasing intrauterine system and breast cancer risk: A systematic review and meta-analysis. Acta Obstet Gynecol Scand. 2020;99(8):970-82.
- 3. Soini T, Hurskainen R, Grenman S, Maenpaa J, Paavonen J, Joensuu H, Pukkala E. Levonorgestrel-releasing intrauterine system and the risk of breast cancer: A nationwide cohort study. Acta Oncol. 2016;55(2):188-92.
- 4. Iversen L, Sivasubramaniam S, Lee AJ, Fielding S, Hannaford PC. Lifetime cancer risk and combined oral contraceptives: the Royal College of General Practitioners' Oral Contraception Study. Am J Obstet Gynecol. 2017;216(6):580 e1- e9.
- 5. 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. Lancet. 1996;347(9017):1713-27.
- 6. Nur U, El Reda D, Hashim D, Weiderpass E. A prospective investigation of oral contraceptive use and breast cancer mortality: findings from the Swedish women's lifestyle and health cohort. BMC cancer. 2019;19(1):807.
- 7. Momenimovahed Z, Salehiniya H. Epidemiological characteristics of and risk factors for breast cancer in the world. Breast Cancer: Targets and Therapy. 2019;11(null):151-64.
- 8. UK Medical Eligibility Criteria for Contraceptive Use (UKMEC): Faculty of Sexual & Reproductive Healthcare. . Clinical Effectiveness Unit; 2016 [updated September 2019; cited 2022 2 July]. Available from: https://www.fsrh.org/standards-and-guidance/documents/ukmec-2016/fsrh-ukmec-full-book-2019.pdf.
- 9. Minalt N, Caldwell A, Yedlicka GM, Joseph S, Robertson SE, Landrum LM, Peipert JF. Association of Intrauterine Device Use and Endometrial, Cervical, and Ovarian Cancer: an Expert Review. Am J Obstet Gynecol. 2023.
- 10. Peipert JF, Zhao Q, Allsworth JE, Petrosky E, Madden T, Eisenberg D, Secura G. Continuation and satisfaction of reversible contraception. Obstet Gynecol. 2011;117(5):1105-13.
- 11. Bofill Rodriguez M, Dias S, Jordan V, Lethaby A, Lensen SF, Wise MR, et al. Interventions for heavy menstrual bleeding; overview of Cochrane reviews and network meta-analysis. Cochrane Database Syst Rev. 2022;5:CD013180.
- 12. Margatho D, Carvalho NM, Bahamondes L. Endometriosis-associated pain scores and biomarkers in users of the etonogestrel-releasing subdermal implant or the 52-mg levonorgestrel-releasing intrauterine system for up to 24 months. Eur J Contracept Reprod Health Care. 2020;25(2):133-40.
- 13. Yucel N, Baskent E, Karamustafaoglu Balci B, Goynumer G. The levonorgestrel-releasing intrauterine system is associated with a reduction in dysmenorrhoea and dyspareunia, a decrease in CA 125 levels, and an increase in quality of life in women with suspected endometriosis. Aust N Z J Obstet Gynaecol. 2018.
- 14. Song SY, Park M, Lee GW, Lee KH, Chang HK, Kwak SM, Yoo HJ. Efficacy of levonorgestrel releasing intrauterine system as a postoperative maintenance therapy of endometriosis: A meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2018;231:85-92.
- 15. Abou-Setta AM, Houston B, Al-Inany HG, Farquhar C. Levonorgestrel-releasing intrauterine device (LNG-IUD) for symptomatic endometriosis following surgery. Cochrane Database Syst Rev. 2013(1):CD005072.
- 16. Gomes MK, Ferriani RA, Rosa e Silva JC, Japur de Sa Rosa e Silva AC, Vieira CS, Candido dos Reis FJ. The levonorgestrel-releasing intrauterine system and endometriosis staging. Fertil Steril. 2007;87(5):1231-4.
- 17. Abbas AM, Samy A, Atwa K, Ghoneim HM, Lotfy M, Saber Mohammed H, et al. The role of levonorgestrel intrauterine system in the management of adenomyosis: A systematic review and meta-analysis of prospective studies. Acta Obstet Gynecol Scand. 2020;99(5):571-81.



Disclaimer:

Family Planning Alliance Australia has taken every care to ensure that the information contained in this publication is accurate and up-to-date at the time of being published. As information and knowledge is constantly changing, readers are strongly advised to confirm that the information complies with present research, legislation and policy guidelines. FPAA accepts no responsibility for difficulties that may arise as a result of an individual acting on this information and any recommendations it contains.