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RESEARCH ARTICLE

HORMONAL CONTRACEPTION AND BREAST CANCER RISK: BALANCING BENEFITS AND VIGILANCE

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Abstract

Hormonal contraception represents one of the most significant advance ments in reproductive health, offering reliable pregnancy prevention and additional benefits such as menstrual cycle regulation and reductio n of certain gynecological cancer risks. However, its potential associati on with breast cancer has been the focus of ongoing research and debate. Current evidence suggests a modest, reversible increase in breast cancer risk during use, with the magnitude of risk influenced by duration of exposure, hormonal formulation, and genetic susceptibility. Progestin-containing methods, whether combined or progestin-only, appear to play a central role although mechanisms involving progestero ne receptor–mediated breast cell proliferation. Women carrying BRCA1/2 mutations may face a greater relative risk, though this must be balanced against the substantial protective effect of hormonal contra ception against ovarian cancer.Despite these associations, the absolute risk for most women remains low. Clinical decision-making should therefore be individualized, integrating patienthistory, genetic backgrou nd, and personal preferences, while ensuring clear communication of both potential risks and health benefits.

Introduction:

Hormonal contraception is one of the major advances in reproductive health, providing highly effective pregnancy prevention while also offering non-contraceptive benefits such as cycle regulation and relief from menstrual pain [1]. Beyond its contraceptive role, it is also prescribed for important medical reasons, including the management of menstrual cycle disorders, endometriosis, and other gynecological conditions. However, its use has sparked ongoing debate about a potential link to breast cancer risk.

Large international analyses indicate that this risk may vary depending on the duration of use, hormonal composition, and timing of exposure [2]. In light of these data, current guidelines recommend an individualized approach to contraceptive choice, tailored toeach woman's risk profile, health status, and personal

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preferences,supported by comprehensive contraceptive counseling to ensure informed and shared decision-making [3].

Breast Cancer Risk in the General Population:

Breast cancer remains the most common cancer among women worldwide, with an estimated 2.3 million new cases diagnosed each year [4]. While most cases occur in women without high-risk genetic mutations, multiple factors, including genetics, reproductive history, and lifestyle; contribute to baseline risk [4]. Hormonal contraception, widely used both for pregnancy prevention and for its non-contraceptive benefits, has been associated with a small and reversible increase in breast cancer risk during use [2].

In 2023, a large meta-analysis by Torres-de la Roche and colleagues combined results from 22 observational studies, including both cohort and case-control designs, conducted between 2015 and 2022 in different countries. Overall, they found that women who had ever used hormonal contraception had about a 33% higher chance of developing breast cancer compared with women who had never used it (OR 1.33; 95% CI: 1.19–1.49). This increase was more noticeable in premenopausal women and in case-control studies. However, the authors emphasized that differences between study designs and populations warrant cautious interpretation [4].

These findings are partly supported by a large Swedish cohort study that followed approximately 1.5 million women for over 14 million person-years. This study found no significant rise in breast cancer risk among users of combined hormonal contraceptives (IRR ≈ 1.03), but did observe a higher risk among women using progestin-only methods (IRR ≈ 1.32). The increased risk was most evident in the first five years of use and gradually returned to baseline within about ten years after discontinuation [5]. Taken together, the evidence suggests that hormonal contraception, particularly progestin-only methods, may slightly increase breast cancer risk, especially with longer use. Nevertheless, the absolute risk remains small and diminishes over time once contraception is stopped [6].

Recent research on long-acting progestin-only contraceptives, such as subdermal implants, depot medroxyprogesterone injections, and levonorgestrel-releasing intrauterine devices (LNG-IUDs), has reported a modest increase in breast cancer risk among premenopausal women, generally in the range of a 20–30% relative risk [1–3]. Large-scale data from the Danish national registry indicated a relative risk of 1.21 (95% CI: 1.11–1.33) for LNG-IUD users [2], corresponding to a small absolute increase of roughly 14 additional cases per 10,000 women over several years of use. This elevated risk appears to decline progressively after discontinuation [6]. Importantly, the absolute risk remains low, particularly in younger women, and must be weighed against the significant non-contraceptive benefits these methods provide, including menstrual regulation and a reduced risk of certain gynecologic cancers [7].

Biologically, progestins appear central to this relationship: prolonged exposure may continuously activate progesterone receptors, stimulating mammary epithelial cell proliferation and potentially favoring the development of more aggressive luminal B tumor phenotypes [8]. They may also enhance breast tissue sensitivity to growth signals, such as epidermal growth factor, thereby accelerating the transition from precancerous lesions to invasive disease [9].

Overall, while hormonal contraceptive use, especially progestin-based methods, may be associated with a modest increase in relative breast cancer risk, the absolute risk increase is small. These findings should be considered alongside the substantial benefits of hormonal contraception, including reliable pregnancy prevention, menstrual cycle regulation, and reduced risk of several gynecologic cancers. For most women, the overall health benefits continue to outweigh the potential risks when contraceptive choices are individualized and periodically reassessed [2–6].

Effect of Duration of Use:

Multiple studies suggest that the relative risk of breast cancer associated with hormonal contraception increases slightly with longer periods of continuous use. Data from the Collaborative Group on Hormonal Factors in Breast Cancer indicate that after 1 to 4 years of use, the risk increase is modest (RR ≈ 1.09, or about 9% higher than in non-users), rising to approximately 1.19 after 5 to 9 years, and reaching about 1.38 after 10 years or more. Importantly, this elevated risk gradually declines after discontinuation, returning close to baseline levels within 5 to 10 years [2].

A recent meta-analysis involving over nine million women confirmed that the slight increase in breast cancer risk linked to hormonal contraception progressively diminishes once the method is discontinued. In most women, the risk returns to a level comparable to that of never-users within about five years. However, in cases of long-term use,particularly beyond a decade,the return to baseline may take closer to ten years. The study also emphasized that the absolute number of additional cases remains small, especially among women under 35 years of age [2,6].

These findings underscore the importance of considering the total cumulative duration of use when counseling on contraception, particularly for women with additional breast cancer risk factors [1].

Biological Mechanisms Linking Hormonal Contraception to Breast Cancer:
Current evidence suggests that the breast cancer risk associated with hormonal contraception is broadly consistent across different delivery methods, including oral pills, implants, injectable formulations, and levonorgestrel-releasing intrauterine systems (LNG-IUS) [6]. A recent large cohort study (Tueley et al., JNCI, 2025) reported an average 25% relative increase in breast cancer risk among users of long-acting progestin-only implants or injectables, confirming earlier meta-analytic findings on progestin-only contraceptives [8].

Progestins, rather than estrogens, appear to play a central role in driving breast epithelial cell proliferation. Recent reviews, such as Kim (2025), highlight that chronic activation of progesterone receptors (PRs) can mediate this proliferative effect [9], potentially favoring the development of more aggressive tumor subtypes like luminal B, characterized by faster growth and a poorer prognosis compared with luminal A tumors [10].

Experimental studies have also shown that progestins can modify the local hormonal environment, enhancing breast tissue sensitivity to growth signals such as epidermal growth factor (EGF), thereby facilitating the progression from precancerous lesions to invasive disease [3,8]. These effects appear to be amplified with prolonged exposure, consistent with epidemiological evidence of a cumulative duration effect on breast cancer risk. Although the absolute risk remains small, these data underscore the need to carefully balance the benefits and risks of progestin-only methods, particularly in women with additional established breast cancer risk factors [6,9].

Hormonal Contraception in Women at High Genetic Risk (BRCA1/BRCA2):
Research shows that hormonal contraception does not affect all women with genetic predispositions in the same way. In a large prospective study, Phillips et al. (2025) found that women carrying a BRCA1 mutation faced a noticeable increase in breast cancer risk, particularly when contraceptives were used for many years. By contrast, no significant association was observed among BRCA2 carriers, suggesting that the two mutations may not respond to hormonal exposure in the same manner [11].

Recent systematic reviews and meta-analyses indicate that the impact of hormonal contraception on breast cancer risk is more pronounced in women carrying a BRCA1 mutation. Studies by van Bommel et al. (2023) [12] and Baranska et al. (2022) [13] suggest that the age at initiation of contraception, particularly after 20 years, as well as cumulative duration of use, influence this risk. Although the absolute increase remains small compared to the already elevated risk associated with BRCA mutations, these findings underscore the importance of individualized contraceptive counseling. The discussion should aim to balance contraceptive efficacy with oncological risk management, ideally within a multidisciplinary framework involving genetics and oncology.

Beyond Current Guidelines: The Role of Epigenetics in Personalized Contraception:
Current contraceptive guidelines are still largely based on general recommendations. However, recent advances in epigenetics and molecular biology open the door to a new way of approaching this issue. Emerging evidence shows that certain biological markers,such as DNA methylation patterns [14], histone modifications, and microRNA expression [15],are associated with early alterations in breast tissue as well as differences in hormonal sensitivity among women.

When these biomarkers are considered alongside well-established risk factors, such as BRCA1/2 mutations [16,17], family history, or reproductive background [18], the concept of a truly personalized contraceptive strategy becomes conceivable. In this model, contraceptive choice would no longer rely solely on standardized guidelines, but rather on the individual's own "biological signature" [19–20]. The goal would be twofold: to ensure effective contraceptive protection while also minimizing the risk of cancer.Although this precision-based approach has not yet

entered routine clinical practice, it represents a promising direction for the next decade in reproductive health and cancer prevention.

Conclusion:

Hormonal contraception is a safe and effective option that not only prevents pregnancy but also helps protect against ovarian and endometrial cancers. While it may slightly raise the risk of breast cancer in some women, especially with BRCA mutations or long use, this risk is usually small and temporary.

In the future, progress in genetics and epigenetics could allow contraception to be tailored to each woman's unique biology. This would make it possible to choose methods that offer strong protection while keeping cancer risks as low as possible.

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