HORMONAL CONTRACEPTIVE USE AND BREAST CANCER RISK: A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: The association between hormonal contraceptive use and breast cancer risk remains unclear due to inconsistent findings influenced by variations in study design, contraceptive formulations, and population demographics.
Objective: This systematic review aims to synthesize existing evidence on the association between hormonal contraceptive use and breast cancer risk, taking into account variations in contraceptive type, duration of use, dosage, and user characteristics.
Methods: Following the PRISMA 2020 guidelines, a comprehensive literature search was conducted across PubMed, ProQuest, Springer, and Google Scholar for studies published between 2021 and 2025. Keywords included "hormonal contraceptive," "breast cancer," and related terms. Inclusion criteria encompassed studies involving women of reproductive age that examined the association between hormonal contraceptive use and breast cancer risk, including observational studies, systematic reviews, and meta-analyses. Studies were screened, duplicates removed, and quality assessed using the Joanna Briggs Institute (JBI) critical appraisal tool.
Results and discussion: Ten eligible studies were reviewed, with mixed findings. Several studies reported a slight but statistically significant increase in breast cancer risk with long-term hormonal contraceptive use, particularly oral estrogen-progestin combinations. The risk appeared to diminish over time following discontinuation. In contrast, some studies found no association, while others suggested potential protective effects under specific conditions, such as in users with a family history of breast cancer. Modern contraceptives with lower estrogen doses may present a different risk profile, though further research is needed.
Conclusion: The Association Between Hormonal Contraceptive Use and Breast Cancer is complex and influenced by multiple variables. While prolonged use may slightly elevate risk, the overall risk remains low and often declines with cessation. Hormonal contraceptives offer notable non-contraceptive benefits and are generally considered safe for most women, including those with genetic predispositions. Informed decision-making should involve individualized risk-benefit analysis, and future research should focus on contemporary contraceptive formulations.

Keywords: Hormonal Contraceptives; Breast Cancer; Systematic Review

Introduction

Breast cancer is one of the most significant public health challenges worldwide. Its incidence continues to rise across various regions, and despite advances in screening, diagnosis, and treatment, global projections indicate a substantial increase in cases over the next two decades (Sung et al., 2021). It remains the most frequently diagnosed cancer among women and is the second leading cause of cancer-related mortality, following cervical cancer. According to the Global Cancer Observatory (GLOBOCAN), approximately 2.3 million new cases of breast cancer are diagnosed annually, resulting in over 685,000 deaths worldwide (WHO, 2022). In many low- and middle-income countries, breast cancer disproportionately affects women of reproductive age and is a primary contributor to cancer-related deaths (Bray et al., 2020).

A wide range of risk factors has been associated with the development of breast cancer, including genetic mutations, reproductive history (e.g., age at menarche, age at first pregnancy, and parity), family history, and lifestyle-related factors such as alcohol intake, obesity, and diet (Li et al., 2021). One area of ongoing debate in the medical and scientific community is the role of hormonal contraceptives, especially combined estrogen-progestin formulations, in influencing breast cancer risk. These contraceptives are among the most commonly used methods of birth control, with an estimated 150 million women using them globally each year (Collaborative Group on Hormonal Factors in Breast Cancer, 2019).

Previous studies have reported conflicting results. Some have suggested a slight but significant increase in breast cancer risk associated with current or recent hormonal contraceptive use, which tends to decline several years after discontinuation (Abbott et al., 2020; Morch et al., 2018). Others have found no clear association, highlighting inconsistencies that may stem from differences in study design, population characteristics, or contraceptive formulations (Beaber et al., 2019; Sundaram et al., 2020).

Given these discrepancies, a comprehensive synthesis of the existing literature is needed. This systematic review aims to consolidate and evaluate the current body of evidence on the association between hormonal contraceptive use and breast cancer risk. By comparing findings across various study types, populations, and contraceptive regimens, this review seeks to clarify the strength and consistency of the association, identify potential risk modifiers, and inform future research and clinical guidelines.

These discrepancies are thought to result from various factors, such as differences in study design (e.g., cohort versus case-control), participant age, parity history, type and dosage of contraceptives used, and methods of exposure measurement. Additionally, the timing and duration of contraceptive use may influence risk estimates, further contributing to inconsistent findings. The situation is further complicated by the fact that many

earlier studies focused on older generations of oral contraceptives, which contained higher doses of estrogen and progestin compared to modern formulations, potentially affecting the applicability of past results to current users.

Estrogen doses (>50 mcg), whereas current formulations generally have lower estrogen content and are available in various forms, including injectables, implants, and intrauterine devices (Morch et al., 2018; Sundaram et al., 2020).

This systematic review aims to synthesize current evidence on the association between hormonal contraceptive use and breast cancer risk, with specific attention to the type, duration, and dosage of contraceptives, to support informed contraceptive decision-making for women of reproductive age.

Methods

Search strategy

The search strategy for this systematic review was conducted and documented by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). A comprehensive literature search was performed using four major scientific databases: PubMed, ProQuest, Springer, and Google Scholar. The keywords employed in the search process included "hormonal contraceptive," OR "contraceptive," AND "breast cancer," combined using Boolean operators such as AND and OR to yield relevant and comprehensive search results. Articles that met the inclusion criteria were selected based on the following considerations: written in English, published between 2021 and 2025, available in full-text format, and classified as original research specifically observational studies (cohort or case-control), systematic reviews, or meta-analyses examining the relationship between hormonal contraceptive use and breast cancer risk.

Inclusion and exclusion criteria

The selection criteria in this systematic review were designed to identify studies that comprehensively and relevantly examine the relationship between hormonal contraceptive use and breast cancer risk. Eligible studies included quantitative research with observational designs (cohort, case-control, or cross-sectional), involving women of reproductive age (15-49 years), written in either Bahasa Indonesia or English, and published in reputable, indexed scientific journals. Additionally, studies were required to present primary data or relevant statistical analyses.

Conversely, studies were excluded if they did not provide essential information regarding hormonal contraceptive use or breast cancer, were only available in abstract form, were classified as non-empirical articles (e.g., narrative reviews or editorials), involved animal or in vitro research, did not meet methodological quality standards, or represented duplicate publications.

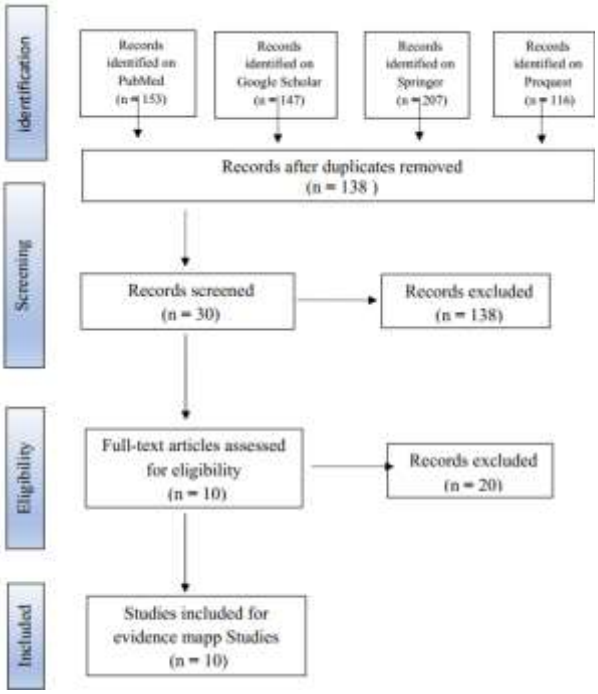

Figure 1. PRISMA Flowchart

Data extraction and risk of bias assessment

The author's name, publication year, research design, participant characteristics, and conclusion about the breast cancer risk associated with hormonal contraceptive usage were extracted.

The data were synthesized narratively by identifying patterns, similarities, and discrepancies across studies about hormonal contraceptive type, duration of use, dosage, and associated breast cancer risk. Key findings, study characteristics, and outcomes were compared and summarized thematically to conclude the strength and direction of associations."

Results

Table 1. *Characteristics and Results of the Included Studies*

Author	Year	Journal	Result
Wahidin, et al.	2018	Asian Pacific Journal of Cancer Prevention	Odds Ratio (OR) of patients using oral contraceptive <6 years was 1.93 (95% CI 1.23 – 3.03) and OR of those using oral contraceptive ≥ 6 years was 2.90 (95% CI 1.65– 5.09) as compared to people who did not use oral contraceptive.
Heikkinen, et al.	2015	Cancer Causes and Control	Regarding use of other hormonal contraceptives (HC), a positive association between long HC use (≥2 years) and BC was observed in both groups, OR being 1.37 (95 % CI 1.12–1.68) for premenopausal and 1.11 (95 % CI 1.03–1.20) for postmenopausal women, when compared to never-users of other HC.
Joukar, et al.	2016	Asian Pacific Journal of Cancer Prevention	Using contraceptives for more than 10 years (OR=2.3; 95% CI=1.4-3.9), family history of other cancers (OR=6.1; 95% CI=1.9-19.3) and a history of X-Ray exposure (OR=4.4; 95% CI=1.07-18.1) were considered as predictive factors.
Nguyen, et al.	2016	International Journal of Breast Cancer	Age at menarche, age at first parity, total months breastfeeding, oral contraceptive use, and menopause were not associated with increased breast cancer risk in this analysis.
Balekouzou, et al.	2017	BMC Women Health	Decreased odds of breast Ca were associated with being employed (AOR = 0.32, CI: 0.19–0.56), living in urban areas (AOR = 0.16, CI: 0.07–0.37), late menarche (AOR = 0.18, CI: 0.07–0.44), regular menstrual cycles (AOR = 0.44, CI: 0.23–0.81), term pregnancy (AOR = 0.26, CI: 0.13–0.50) and hormonal contraceptive use (AOR = 0.62, CI: 0.41–0.93).
Morch, et al.	2017	The New English Journal of Medicine	After discontinuation of hormonal contraception, the risk of breast cancer was still higher among the women who had used hormonal contraceptives for 5 years or more than among women who had not used hormonal contraceptives. Risk estimates associated with current or recent use of various oral combination (estrogen–progestin) contraceptives varied between 1.0 and 1.6
Dianatinasab, et al.	2017	Clinical Breast Cancer	oral contraceptive usage (OR 1.46; 95% CI, 1.05-2.04), physical inactivity (OR, 1.54; 95% CI, 1.39-1.75), past life stress (OR, 2.40; 95% CI, 1.62-3.56), and regular bedtime (OR, 0.32; 95% CI, 0.19-0.54) were related to a higher risk of breast cancer
Jareid, et al.	2017	Gynecologic Oncology	Among ever users of LNG-IUS there were 18 cases of epithelial ovarian cancer, 15 cases of endometrial cancer, and 297 cases of breast cancer. Whenever users were compared to never users of LNG-IUS, the multivariable RR of ovarian, endometrial, and breast cancer was 0.53 (95% CI: 0.32, 0.88), 0.22 (0.13, 0.40), and 1.03 (0.91, 1.17), respectively.
Chaveepojnkamjorn, et al	2017	Asian Pacific Journal of Cancer Prevention	women with oral contraceptive use increased the risk of breast cancer by a factor of over 3 times (OR=3.39, 95%CI =1.98-5.75). In addition, the greater the duration of oral contraceptive, the greater the risk (OR 6-10 yrs=3.91, 95%CI = 1.99-7.64, OR >10 yrs=4.23 95%CI = 2.05-8.71)
Wahidin, et al.	2018	Asian Pacific Journal of Cancer Prevention	Odds Ratio (OR) of patients using oral contraceptive <6 years was 1.93 (95% CI 1.23 – 3.03) and OR of those using oral contraceptive ≥ 6 years was 2.90 (95% CI 1.65– 5.09) as compared to people who did not use oral contraceptive.

Disccusion

The results of this systematic review reveal ongoing controversy regarding the association between hormonal contraceptive use and breast cancer risk. While earlier studies, such as those by Marchbanks et al. (2002) and Wingo et al. (2000), found no statistically significant association, more recent data suggest a modest but measurable increase in risk, particularly with current or prolonged use of modern combined oral contraceptives (Anothaisintawee et al., 2013; Del Pup et al., 2013; Gierisch et al., 2013). These findings align with the biological plausibility that estrogen and progestin may exert mitogenic effects on breast tissue,

promoting proliferation and potentially contributing to tumorigenesis in genetically susceptible individuals (Li et al., 2021).

However, it is essential to emphasize that the absolute increase in breast cancer risk remains low, and must be interpreted within the context of individual patient profiles and broader health outcomes. Hormonal contraceptives offer numerous non-contraceptive benefits, including regulation of menstrual cycles, treatment of endometriosis, acne reduction, and even decreased risks of ovarian and endometrial cancers (WHO, 2022; Burkman et al., 2004). These advantages are especially relevant for women with chronic health conditions or those transitioning through reproductive aging, where newer delivery systems (e.g., intrauterine or subdermal implants) provide improved safety and convenience.

Conflicting evidence from high-quality observational studies and meta-analyses reflects the complexity of isolating the impact of hormonal contraceptives on breast cancer development. Factors such as age at initiation, duration of use, formulation type, genetic background (e.g., BRCA1/2 mutations), body mass index, and physical activity level appear to influence the risk differently across populations. For instance, estrogen levels may be modulated by lifestyle choices like exercise, which in turn can attenuate the associated cancer risk, as suggested by epidemiologic data (Friedenreich et al., 2010; Monninkhof et al., 2007). Furthermore, the role of obesity as both a side effect of hormonal contraceptives and an independent risk factor for breast cancer complicates causal attributions (Lauby-Secretan et al., 2016).

Some recent research has challenged the assumption of a linear risk profile. Vessey and Painter (1990) suggested that users of oral contraceptives may present with less advanced-stage tumors, potentially due to increased health surveillance or hormonal influence on tumor biology. Moreover, findings by Moradzadeh et al. (2020) imply that a family history of breast cancer may modify the association, possibly offering a paradoxical protective effect when combined with long-term contraceptive use. This finding remains controversial and underlines the need for stratified analyses in future studies.

It is also notable that several ethnic subgroups exhibit different risk levels. While Anothaisintawee et al. (2013) reported a slightly higher relative risk among Asian women compared to Caucasians, the confidence intervals overlapped, suggesting no statistically significant difference. This highlights the importance of considering ethnicity, genetic factors, and regional healthcare access when interpreting epidemiological data.

Given the variability of outcomes and methodological limitations in many included studies—such as recall bias in case-control designs and residual confounding in cohort studies—there remains a need for large-scale, prospective, multiethnic cohort studies with standardized exposure measurement. Integrating molecular and genetic profiling may also yield more personalized risk

assessments in the future (Hunter et al., 2005).

Conclusion

This systematic review highlights the complex and nuanced relationship between hormonal contraceptive use and breast cancer risk. While several studies indicate a slight increase in risk—particularly with prolonged or current use—this risk appears to diminish over time after discontinuation. The inconsistencies in findings across studies can be attributed to differences in study design, population characteristics, and types and formulations of contraceptives used.

Despite these concerns, hormonal contraceptives offer significant non-contraceptive benefits and are generally considered safe for most women, including those with a family history of breast cancer. The introduction of newer contraceptive formulations with lower estrogen doses emphasizes the need for up-to-date research to evaluate their safety profiles.

In conclusion, the current evidence suggests that the risk associated with hormonal contraceptive use is modest and must be balanced against its benefits. Decisions regarding contraceptive use should be based on a personalized assessment of risks and advantages, taking into account individual medical history, preferences, and lifestyle factors. Further large-scale, well-designed studies are essential to better understand the risks associated with modern contraceptive methods.

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