

REVIEWER'S REPORT

Manuscript No.: IJAR-53568

Date: 26-08-2025

Title: Hormonal Contraception and Breast Cancer Risk: Balancing Benefits and Vigilance

Recommendation:

Accept as it is
 Accept after minor revision.....✓.....
 Accept after major revision
 Do not accept (*Reasons below*)

Rating	Excel.	Good	Fair	Poor
Originality		✓		
Techn. Quality		✓		
Clarity			✓	
Significance		✓		

Reviewer Name: Shashi Prakash

Date: 27-08-2025

Reviewer's Comment for Publication.

(To be published with the manuscript in the journal)

The reviewer is requested to provide a brief comment (3-4 lines) highlighting the significance, strengths, or key insights of the manuscript. This comment will be Displayed in the journal publication alongside with the reviewers name.

This article offers a thorough and current synthesis of evidence relating hormonal contraception to breast cancer risk. It weighs epidemiological evidence, biological mechanisms, and genetic susceptibility against careful consideration of clinical decision-making. The novel integration of the emerging view on personalized contraception based on epigenetic markers enhances novelty and significance.

Detailed Reviewer's Report

The abstract is efficient in summarizing main points but reads a little dense and too technical for readers skimming through the paper. Simplify sentence structure, state in clearer terms that absolute risk remains small even with relative risk alterations, and clearly state that the rise is reversible. The addition of a concluding sentence on the imperative for individual counselling would enhance impact.

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Introduction section is well contexted with proper references. Some sentences are too long and may be shortened for easy readability. It would be helpful to state clearly at the beginning that the absolute risk increase is minimal to prevent misinterpretation. Providing a transition sentence that gives an overview of the structure of the manuscript (epidemiology → mechanisms → high-risk groups → personalized approaches) would direct readers.

Breast Cancer Risk in the General Population

The section is comprehensive and data-rich but a little tedious to read. It may help to put relative and absolute risk numbers side by side in a clear table for easy understanding. Also, make the reporting of study outcomes (IRR, RR, OR) consistent and clearly explain their interpretation to non-specialists. Including a mention of how confounding variables (e.g., history of reproduction, obesity) were handled in key studies would make the critical appraisal more robust.

Effect of Duration of Use

Good explanation of cumulative risk, but the text can be condensed. Think of comparing risks briefly between short-term versus long-term use in one summarizing sentence. A graphical figure displaying risk over time would be useful. Make sure referencing style is consistent and avoid duplicating data previously stated in previous sections.

Biological Mechanisms Linking Hormonal Contraception to Breast Cancer

This section is didactic and brings out the role of progestins nicely. Mechanistic discussion, however, could be too elaborate for a general clinical audience. Explain experimental results in easier language and underscore how these mechanisms correlate with epidemiological information. Including a brief statement indicating that these results are biologically plausible but not conclusive would prevent overreading.

Hormonal Contraception in Women at High Genetic Risk (BRCA1/BRCA2)

The risk discussion for BRCA is solid and well-referenced, although the combination of French and English sentences must be translated into English for consistency. Brief mention can be made that although relative risk increases in BRCA1 carriers, there is a large protective effect against ovarian

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cancer, which will influence risk–benefit discussions. A sentence indicating current guideline recommendations for BRCA carriers would be useful.

Beyond Current Guidelines: Epigenetics and Personalized Contraception

This is the most innovative section of the manuscript, but is written more as an opinion than a review. Shorten the discussion a bit, give specific examples of possible biomarkers, and stipulate that this methodology is only hypothetical currently. A sentence indicating priorities for research (e.g., prospective studies, cost-effectiveness) would make this section more practical.

Conclusion paragraph is well said but could be stronger. Reinstate the key message that absolute breast cancer risk is low and reversible, and that one-to-one counselling is essential. Last sentence on epigenetics is encouraging but would be strengthened by a guarded statement noting that this is not currently in general practice.