Factors Associated with Breast Cancer Risk in Women: A Literature Review

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Abstract: Breast cancer is a disease with a multifactorial etiology shaped by genetic, hormonal, reproductive, phenotypic, environmental, and socio-behavioral determinants. This narrative review with a systematic search strategy aimed to systematize factors associated with breast cancer risk and incidence, with an emphasis on their applicability in risk-oriented early detection models. The literature search was conducted in PubMed/MEDLINE, Scopus, eLIBRARY.ru, and additional sources for the period from 19 December 2020 to 19 December 2025. The review included narrative reviews, systematic reviews, and meta-analyses, as well as a limited number of original studies meeting predefined eligibility criteria (Population, Exposure, Outcome, and Study design). The final corpus comprised 48 publications. Risk factors were grouped into thematic domains and qualitatively classified according to the degree of epidemiological consistency and suitability for inclusion in individual risk models (categories A–C). The most robust associations were identified for age, mammographic density, hereditary and family history, several hormonal and reproductive characteristics, smoking, and night shift work. For environmental exposures, obesity, and certain chemical factors, the evidence base was characterized by greater heterogeneity, whereas for psychoemotional factors and radiofrequency electromagnetic fields it remained limited and should be considered hypothesis-generating. This review demonstrates the uneven quality and consistency of contemporary evidence on breast cancer risk factors and highlights the need for their critical interpretation within risk-oriented approaches. The resulting list of candidate factors may serve as a basis for predictor selection and subsequent prospective validation in the development of individual risk models aimed at optimizing early diagnosis.

Keywords: Breast cancer, breast cancer risk factors, breast cancer screening, breast cancer diagnosis, epidemiology, etiology, risk stratification, individual risk model.

INTRODUCTION

Breast cancer (BC) is characterized by a multifactorial etiology, with the probability of its development shaped by genetic, hormonal, metabolic, environmental, and other determinants. The literature indicates that breast cancer risk factors differ in both the strength of their associations and the presumed mechanisms of action. Evidence is consistent for some determinants, whereas other areas require further clarification.

In contemporary oncology, increasing attention is being paid to the preclinical stages of carcinogenesis and to opportunities for earlier disease detection [1-3]. This trend shifts the focus from uniform screening approaches toward risk-stratified strategies, in which the accurate selection of risk predictors becomes a key element. In the context of developing risk-oriented approaches to the early detection of breast cancer, the systematization of factors associated with disease risk has practical significance for the subsequent construction and refinement of individual risk models.

Accordingly, this review maps and systematizes contemporary evidence on breast cancer risk factors to support subsequent selection of predictors for risk-oriented early detection models.

MATERIALS AND METHODS

The literature search was conducted in PubMed/MEDLINE, with the final search date set at 19 December 2025. The inclusion time frame was limited to the most recent five years (19 December 2020–19 December 2025). To identify relevant publications in PubMed, the following search strategy was applied:

("Breast Neoplasms/etiology"[Majr] OR "Breast Neoplasms/epidemiology"[Majr]) AND ("Risk Factors"[Majr] OR risk factor[ti] OR "cancer risk"[ti] OR susceptibility[ti] OR incidence[ti]) AND (Review[pt] OR "Systematic Review"[pt]) NOT (metasta*[ti] OR metastatic[ti] OR recurren*[ti] OR relaps*[ti] OR prognos*[ti] OR survival[ti] OR surviv*[ti] OR survivorship[ti]) AND ("2020/12/19"[Date - Publication] : "2025/12/19"[Date - Publication]). This query yielded 169 records.

To identify publications not indexed in PubMed, we additionally searched eLIBRARY.ru (19 December 2025) and Scopus (21 December 2025). Manual

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searches were also performed in DOAJ and RusMed and by screening reference lists (19 December 2025). For databases outside PubMed, reproducible search queries were used: in Scopus (TITLE-ABS-KEY field) — ("breast cancer" OR "breast neoplasms") AND ("risk factor" OR incidence OR susceptibility), with filters applied for the years 2020–2025 and publication types Review/Systematic Review/Meta-analysis; in eLIBRARY.ru — searches across the "title/abstract/keywords" fields using the terms "рак молочной железы" AND "факторы риска," with filters for 2020–2025 and publication types "review/systematic review/meta-analysis." Manual searches (DOAJ, RusMed, and bibliographies of included articles) were used to identify additional relevant studies; such publications were included only if they fully met the predefined eligibility criteria (Population, Exposure, Outcome, and study design).

In total, 244 records were identified (PubMed, n = 169; non-PubMed sources—Scopus/eLIBRARY/manual search, n = 75). After removal of duplicates (n = 60), 184 records remained for screening. Of these, 80 articles underwent full-text assessment, and 32 were excluded (main reasons: irrelevant outcome, inappropriate publication type, or publication period). The final review corpus comprised 48 publications.

Source selection was conducted in stages: the first stage involved screening of titles and abstracts, followed by full-text assessment for eligibility. Predefined inclusion criteria were applied during title/abstract screening and full-text assessment. Inclusion decisions were based on Population, Exposure, Outcome, and study design, as well as relevance to breast cancer risk/incidence.

Inclusion Criteria

- Population: Women.
- Exposure: Any factors/exposures potentially associated with the risk of developing breast cancer.
- Outcome: Breast cancer risk/incidence (etiology/epidemiology).
- Study design: For the primary analysis—narrative reviews, systematic reviews, and meta-analyses; contextually, original studies were included when necessary to clarify mechanisms, regional characteristics, or exposure parameters.
- Timeframe: 19 December 2020 – 21 December 2025.
- Results: Publications examining the association between an exposure and breast cancer risk/incidence were included, encompassing positive, null, and conflicting findings.

Exclusion Criteria

- Irrelevant outcomes (metastasis, recurrence, survival, survivorship);
- Inappropriate publication types (case reports, editorials, letters, opinions/commentaries, etc.);
- Population criteria (studies focusing on transgender men were not included and were not analyzed separately);
- Publication period outside 19 December 2020 – 21 December 2025.

The review followed a narrative approach with a systematic search strategy and was aimed at structuring and comparing thematic blocks of breast cancer risk factors, primarily based on data from secondary sources (systematic reviews and meta-analyses). Formal quality assessment (e.g., using risk-of-bias tools) and quantitative re-estimation of effect sizes for individual factors were not objectives of this work. Accordingly, the conclusions of the review should be regarded as a foundation for identifying candidate factors and for subsequent prospective validation prior to practical implementation in risk-based models.

RESULTS

Based on the search and selection process, a body of publications was assembled and systematized by factor domains: genetic; hormonal and reproductive; phenotypic; and socio-behavioral factors. The structure and robustness of evidence across these domains were heterogeneous. For risk-oriented interpretation, factors were additionally classified according to their suitability for inclusion in individual risk models: A—robust associations supported by multiple systematic reviews/meta-analyses (SR/MA) and/or large cohort studies; B—probable or context-dependent associations characterized by heterogeneous results; C—insufficient or conflicting epidemiological evidence (predominantly mechanistic or limited observational data).

Decision rules for the A–C categorization. The A–C categorization represents a qualitative evidence-mapping framework used to prioritize candidate predictors for risk-model development. Categories were assigned using three main considerations: consistency

across recent systematic reviews/meta-analyses, breadth of the supporting evidence base, and comparability of exposure definitions and outcomes (breast cancer risk/incidence) across studies. Category C was treated as hypothesis-generating and was not considered suitable for inclusion in risk models without additional validation. This framework does not represent a formal GRADE assessment.

Genetic and hormonal–reproductive determinants were the most consistently represented domains. The genetic block includes syntheses of high-risk hereditary variants (including BRCA1/2 and DNA repair genes) as well as meta-analytic estimates of selected polymorphisms. The hormonal–reproductive block encompasses reproductive history characteristics and hormonal interventions, including data from meta-analyses and systematic reviews on the duration of hormonal contraceptive use. Phenotypic factors—most notably mammographic breast density—are presented as consistently discussed risk predictors; for mammographic density, systematic reviews and meta-analyses have been published, including in specific contexts (e.g., benign breast disease).

The environmental domain is characterized by greater heterogeneity. Alongside narrative and mechanistic reviews on endocrine-disrupting compounds, meta-analytic assessments of specific chemical exposures (e.g., bisphenol A and phthalates) are available, whereas the most methodologically consolidated epidemiological evidence pertains to ambient air pollution (systematic reviews of longitudinal studies and meta-analyses). Systematized data on inorganic contaminants (arsenic and gene–arsenic interactions) are presented separately, as are original studies used to contextualize household and territorial exposure pathways (household dust; landscape-geochemical and geological characteristics of regions).

Among modifiable factors, the most systematized evidence relates to night shift work and smoking, including meta-analytic syntheses addressing dose–response relationships and passive smoking. For diet, systematic reviews of region-specific evidence and a meta-analysis on ultra-processed food consumption are presented; obesity is discussed primarily in a narrative review with consideration of potential molecular mechanisms. Psychoemotional factors are covered to a limited extent and predominantly at the level of original studies and applied models and should be interpreted as emerging/hypothesis-generating evidence.

For ease of interpretation, the main systematic reviews and meta-analyses for each risk factor group and subgroup are summarized in Table **1**.

Within the framework of risk-oriented interpretation, factors were conditionally allocated to categories reflecting their suitability for inclusion in individual risk models. Category A comprises the most robustly supported candidates, including age, mammographic density, familial/genetic risk, several hormonal and reproductive factors, as well as smoking and night shift work. Category B includes candidates with a more variable or context-dependent evidence base, such as ambient air pollution, selected chemical exposures, and obesity. Category C encompasses factors with a limited or uncertain overall weight of evidence, including psychoemotional stress and radiofrequency electromagnetic fields.

DISCUSSION

The presented data confirm that breast cancer is a multifactorial disease and that the relative “weight” of different risk determinants is heterogeneous.

Genetic Factors

Hereditary predisposition is regarded as one of the most firmly established components of breast cancer risk. Pathogenic variants in BRCA1/2 and other DNA repair genes are associated with an increased probability of breast cancer development and with an earlier age at disease onset [4, 5, 6]. In addition, the contribution of other genetic variants has been discussed: in Asian populations, the polymorphisms rs11549465 C/T and rs11549467 G/A have been associated with an increased risk of breast cancer [7], while in populations of European ancestry the XRCC2 Arg188His polymorphism [8] and the CXCL12 rs1801157 polymorphism [9] have been reported to confer elevated risk.

Ethnicity-specific variants may modify genetic risk estimates [10]. Genetic determinants should therefore be interpreted alongside environmental and socio-behavioral factors.

Hormonal and Reproductive Factors

Hormonal influences occupy a central position among endogenous determinants of breast cancer risk. Prolonged estrogen exposure—such as late menopause [11], nulliparity [12], shorter duration of lactation [13], and the use of hormonal medications—

Table 1: Summary of Breast Cancer Risk Factors and their Suitability for Inclusion in Individual Risk Model

Factor group	Exposure (subgroup)	Key syntheses (first author, year)	Type	Direction of association[1]	Model category (A/B/C)[2]	Routine measurability[3]	Quantitative estimate (CI available)[4]	Approx. risk magnitude
Phenotypic	Age	— (established risk factor)	—	↑	A	easy	NA	strong
	Mammographic density	Bodewes, 2022; Bai, 2024	SR/MA[5]; SR/MA	↑	A	partial (mammography)	CI	moderate–strong
	Benign breast disease (BBD[6])	Burke, 2025	SR	↑	A/B	partial (medical records)	NR	moderate
Genetic	Polymorphisms (candidate genes)	Islam, 2022; Alijanpour, 2024; Dastgheib, 2024	MA; MA; SR/MA	↑ (for specific variants)	B	difficult/partial (genotyping)	CI	small / variant-specific
	Family history / high-penetrance hereditary mutations (*BRCA*, etc.)	Pavlova, 2024; Obeagu, 2024	review	↑	A	partial (history/genetic testing)	NR	strong (subgroup-specific)
Hormonal / reproductive	Parity (including tumor subtypes)	Li, 2021	SR/MA	↕	A/B	easy	CI	variable
	Hormonal contraception (duration)	Sayon-Orea, 2025	SR/MA	↑	A	easy (history/prescriptions)	CI	small–moderate
	Menopausal hormone therapy: estrogen-only (RCT data)	Chlebowski, 2024	MA (RCTs[7])	0	A	easy (prescriptions)	CI	small / none
	Levonorgestrel-releasing IUD[8]	Zürcher, 2023	SR	↑?	B	easy (prescriptions)	NR	small / uncertain
Environmental	Ambient air pollution (longitudinal data/meta-analyses)	Tippila, 2024; Gabet, 2021; Wang, 2025	SR; MA; MA	↑	B	difficult (exposure modeling)	CI	small / variable
	Ionizing radiation (occupational exposure)	Martello Cristófalo, 2025	SR/MA	↑	B	partial (occupational history/dose)	CI	small–moderate
Socio-behavioral	Night shift work	Wei, 2022	MA	↑	A/B	partial (occupational history)	CI	small–moderate/ variable
	Smoking (active)	Scala, 2023	SR/MA	↑	A	easy	CI	small–moderate
	Passive smoking	Possenti, 2024	SR/MA	↑	A/B	partial	CI	small
	Diet: ultra-processed foods	Karimi, 2025	SR/MA	↑	B	difficult/partial	CI	small–moderate/ variable
	Dietary factors (regional evidence, MENA[9])	Lamchabbek, 2025	SR	↕	B/C	difficult/partial	NR	variable / uncertain

[1]Direction of association: ↑ increased risk; ↓ decreased risk; 0 no consistent association; ↑? probable/context-dependent association; ↕ — heterogeneous/mixed findings across studies.
[2]Model category: A — high suitability; B — probable/context-dependent (requires exposure refinement and validation); C — limited or conflicting evidence (hypothesis-generating, insufficient for routine model inclusion without further validation).
[3]Routine measurability: easy — medical history/standard data; partial — dependent on availability of records, screening, or registries; difficult — requires exposure modeling or specialized measurements.
[4]Quantitative estimate (CI available): CI — effect estimate with 95% confidence interval reported; NR — not reported; NA — not applicable.
[5]SR — systematic review; MA — meta-analysis; SR/MA — systematic review and meta-analysis.
[6]BBD — benign breast disease.
[7]RCT — randomized controlled trial.
[8]IUD — intrauterine device (levonorgestrel-releasing).
[9]MENA — Middle East and North Africa.

has been associated with an increased likelihood of breast cancer [14, 15]. According to a systematic review and meta-analysis of cohort studies, long-term (≥5 years) use of hormonal contraceptives is associated with an increased risk of breast cancer [16].

With respect to menopausal hormone therapy, the literature also describes a positive association with breast cancer risk, predominantly for combined and/or certain non–estrogen-only regimens; by contrast, estrogen-only therapy generally does not demonstrate a statistically significant increase in risk [17-19]. In addition, some studies have reported a positive association between the use of a levonorgestrel-releasing intrauterine system and breast cancer risk [18].

Among exogenous influences, xenoestrogens—chemical compounds capable of interacting with estrogen receptors and mimicking hormonal signaling—represent an important group of exposures [20]. The overlap of endogenous and exogenous hormonal effects complicates the assessment of the contribution of reproductive factors and underscores the need for an integrated consideration of hormonal and environmental components.

Phenotypic Factors and Age

Age is among the most consistently confirmed risk factors: across all populations, the incidence of breast cancer increases with advancing age. At the same time, interpretation of incidence trends should take demographic processes into account, as changes in age-standardized rates are often linked to population aging [10].

In addition to age, mammographic breast density represents a significant risk predictor [21-23].

Environmental Factors

Environmental determinants of breast cancer risk are actively studied in carcinogenesis research, particularly in regions with a pronounced technogenic burden. Among external carcinogens, polycyclic aromatic hydrocarbons (PAHs) remain the most extensively studied; these compounds are capable of affecting estrogen-dependent signaling pathways and stimulating proliferative processes in breast tissue [24]. Factors potentially influencing hormonal balance and breast cancer risk include endocrine disruptors—such as bisphenol A, polychlorinated biphenyls, and certain pesticides [20, 25]. In addition, the literature describes a possible role of phthalates, which possess estrogen-mimicking properties and may enhance proliferative activity [26-28].

Epidemiological evidence indicates the importance of ambient air pollution: a systematic review of longitudinal studies identified an association between exposure to air pollutants and an increased risk of breast cancer [29]. These findings are consistent with meta-analytic data showing that reduced long-term exposure to NO_2 (or correlated pollutants) is associated with a lower risk of breast cancer [30, 31]. Beyond atmospheric exposure, a systematic review has reported a possible association between arsenic exposure and breast cancer risk, particularly in studies assessing metabolites and/or genetic–epigenetic interactions [32].

Household sources of chemical exposure are discussed separately: differences in the chemical composition of household dust between women with breast cancer and control groups have been proposed as a potential marker of the relevance of everyday exposure pathways [33].

The literature also highlights landscape–geochemical characteristics of regions, suggesting that higher breast cancer risk may be associated with areas characterized by unfavorable geochemical conditions [34]. In addition, a potential protective role of natural ecosystems—primarily forested areas—is discussed, as they may serve as a marker of a more favorable environmental setting and/or lower exposure to pollutants [35].

Ionizing radiation is a recognized risk factor: a meta-analysis demonstrated an increased risk of breast cancer among female physicians occupationally exposed to radiation sources [36].

Socio-Behavioral Factors

Among modifiable determinants, work schedule characteristics play an important role: night shift work has been associated with an increased risk of breast cancer [37,21]. Review literature has also demonstrated an association between tobacco smoking and breast cancer risk, including dose-dependent effects; among non-smoking women, passive smoking has likewise been associated with an elevated risk [38-40].

Dietary and behavioral factors constitute a separate group. Reviews identify high-fat diets, alcohol

consumption, and low physical activity as determinants of increased breast cancer risk. At the level of dietary habits and patterns in the MENA region, associations appear to be multidirectional: lower risk has been linked to higher consumption of fruits and vegetables, fish/seafood, and black tea, whereas higher risk has been associated with the consumption of milk and white bread. With respect to dietary patterns, protective associations are more frequently reported for Mediterranean and "healthy" plant-based/antioxidant-rich patterns, while increased risk has been observed for diets characterized by high insulinemic load, high glycemic index, and pro-inflammatory profiles [41]. A meta-analysis has also demonstrated an association between high consumption of fast food and ultra-processed foods and an increased risk of breast cancer [42].

Obesity is considered an independent modifiable risk factor for breast cancer; potential miRNA-mediated mechanisms have been discussed [43]. In certain clinical cohorts, statistically significant associations are not observed for some modifiable factors.

A number of studies have examined the contribution of psychoemotional characteristics to breast cancer risk [44, 45]; however, it is emphasized that the evidence base in this area remains limited and is predominantly derived from observational studies, and should therefore be interpreted as hypothesis-generating rather than conclusive.

LIMITATIONS

This review has several limitations. The included studies differ in quality and design, as well as in exposure definitions, assessment methods, and population characteristics, which may to some extent affect the comparability and generalizability of the results. In addition, the level of development of the evidence base varies across different groups of risk factors: for some determinants, large-scale epidemiological syntheses are available, whereas for others the evidence is derived mainly from mechanistic or limited observational studies. For emerging exposures (e.g., selected chemicals, psychoemotional factors, and radiofrequency EMF), conclusions are limited by heterogeneous exposure definitions and predominantly observational evidence, and should be treated as hypothesis-generating.

Despite the use of multiple bibliographic databases and manual searching, the possibility of publication bias cannot be fully excluded.

CONCLUSION

Evidence on breast cancer risk factors published in 2020–2025 is heterogeneous. Systematic reviews and meta-analyses are available for some determinants, whereas for others the evidence relies mainly on mechanistic and/or observational data. This limits causal inference and reduces comparability across populations. For risk-oriented early detection, predictor selection therefore requires consideration of both association strength and the underlying evidence base.

Recent literature increasingly addresses a broadening range of exposures under consideration, in parallel with technological change and evolving consumption patterns. Recent publications report increasing interest in emerging contaminants—insufficiently regulated chemical compounds of domestic and industrial origin—which may be regarded as emerging, hypothesis-generating evidence. Although potential long-term effects of such exposures, including a possible contribution to carcinogenesis, have been highlighted in recent literature, they remain incompletely characterized and require further verification [46]. At the same time, several areas persist in which the overall weight of evidence remains uncertain. For radiofrequency electromagnetic fields, the evidence is considered weak or inconclusive due to data gaps and substantial methodological heterogeneity across studies [47]. For psychological stress, prospective data do not support a consistent association with cancer incidence, with the certainty of evidence remaining very low [48]. Taken together, these observations indicate that some contemporary risk hypotheses relate either to relatively "young" exposures in terms of duration or to insufficiently standardized definitions and measurement approaches, thereby constraining the accumulation of comparable evidence.

From a practical perspective, these findings may inform priorities for future research. Well-designed prospective studies with harmonized exposure definitions, more precise quantitative assessment (including dose–time characteristics), and adequate control for confounding are required to clarify the contribution of individual factors and their potential interactions. The list of candidate factors compiled in this review, together with their qualitative classification by consistency and applicability, may be used for the initial selection of predictors when developing or updating individual breast cancer risk models aimed at optimizing early detection. For factors classified as categories B–C, further standardization of exposure

parameters and prospective validation are necessary before their incorporation into risk-oriented early detection algorithms. Overall, this review serves to structure and compare the available evidence across key domains of breast cancer risk factors and provides a framework for the development and validation of risk-oriented approaches to early breast cancer detection.

INFORMED CONSENT

This study is a review; therefore, informed consent is not required

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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AUTHORS' CONTRIBUTIONS

Anastasia Anichkova: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing – Original Draft, Writing – Review & Editing.

Shamil Kzyrgalin: Supervision, Methodology (oversight), Resources, Validation, Writing – Review & Editing, Final approval of the manuscript.

Rustem Khasanov: Supervision, Project administration, Writing – Review & Editing, Final approval of the manuscript.

Shamil Gantsev: Supervision, Validation, Writing – Review & Editing, Final approval of the manuscript.

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