Feb 20, 2026

In silico approaches used to study BRCA1 and BRCA2 variants in breast cancer: A Systematic review

DOI
https://dx.doi.org/10.17504/protocols.io.bp2l6ep65gqe/v1

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DOI: https://dx.doi.org/10.17504/protocols.io.bp2l6ep65gqe/v1

Protocol Citation: JABRI Zineb, BOUTIB Amal 2026. In silico approaches used to study BRCA1 and BRCA2 variants in breast cancer: A Systematic review. **protocols.io** https://dx.doi.org/10.17504/protocols.io.bp2l6ep65gqe/v1

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Protocol status: Working
We use this protocol and it's working

Created: February 17, 2026

Last Modified: February 20, 2026

Protocol Integer ID: 243548

Keywords: brca2 variants in breast cancer, tumour suppressor genes brca1, brca1 gene, brca2 gene, brca2 gene5, brca2 variant, brca1, tumor suppressor gene, brca23, breast cancer, various mutation, most of the mutation, mutation, systematic review breast cancer, most breast cancer case, due to various mutation, genetic susceptibility2, due to genetic susceptibility2, cancer in women, point mutation, gene, diagnosed cancer, dna repair, large genomic rearrangement, homologous recombination

Abstract

Breast cancer (BC) is the most frequently diagnosed cancer in women worldwide, with 2 million new cases diagnosed each year[1]. Most breast cancer cases are sporadic. However, it is estimated that 5-10% of cases are due to genetic susceptibility[2]. This vulnerability is majoritarily due to various mutations in the two tumour suppressor genes BRCA1 and BRCA2[3]. In fact, women who inhereited and carry these mutations are more at risk of developing the disease when compared with the general population[4].

The BRCA1 and BRCA2 genes are tumor suppressor genes involved in DNA repair, by regulating the homologous recombination (HR). Currently, more than 1600 and 1800 mutations have been identified respectively in BRCA1 gene and BRCA2 gene[5]. These genes are 83 and 86 kb long with coding sequences of 5.7 and 10.2 kb, scattered over 22 and 26 coding exons[6]. Most of the mutations identified are point mutations and small insertions/deletions. Additionnaly, large genomic rearrangements have also been identified.

In silico approaches consist of studying these variants using computer modelling and/or computer simulation. It is still unclear how diverse these methods are and on what they are implemented. Our systematic review aims at providing a comprehensive overview of all the current in-silico approaches and studies performed on BRCA1 and BRCA2 variants as well as their results. In other words, our systematic review could help researchers gain an understanding of the current in-silico methods, procedures and methods as well as their respective results.

Before start

Research Question(s):

PICO:
- **Population:** BRCA1 and BRCA2 gene variants in breast cancer.
- **Intervention:** In silico methods, approaches and procedures.
- **Comparison:** No comparison.
- **Outcome:** Results of characterization and interpretation of BRCA1 and BRCA2 variants.

Eligibility Criteria (Inclusion/Exclusion):

Inclusion Criteria:
- **Population/Participants:** BRCA1 and BRCA2 variants in breast cancer patients.
- **Intervention/Exposure:** In-silico methods, approaches and procedures used to study BRCA1 and BRCA2 variants in breast cancer patients.
- **Outcomes:**
  - To provide a comprehensive overview of all the current in-silico approaches, methods and procedures used to study BRCA1 and BRCA2 variants.
  - To enumerate the different areas of research covered by the in-silico studies.
  - To outline future perspectives and emerging trends in this field.
- **Study design:**
  - Experimental in-silico studies.
  - Primary computational studies.
  - Comparative computational studies.
  - Method development studies.
  - Validation studies.
- **Time frame:** The last 20 years.
- **Language:** No restrictions.
- **Article specifications:**
  - Results should present interpretable outcomes.
  - The methodology must be clearly explained.
  - The publication should be peer-reviewed, and the full text must be accessible for thorough evaluation.

Exclusion Criteria:
- **Population/Participants:** Other gene variants.
- **Intervention/Exposure:**
  - Non-In-Silico approaches and methods used to study BRCA1 and BRCA2 variants in breast cancer.
  - In-silico approaches and methods used to study BRCA1 and BRCA2 variants in other types of cancers such as ovarian cancers.
  - In silico approaches and methods used to study other gene variants in breast cancer or in other types of cancers.

- **Outcomes:** The review does not aim to propose new in-silico methods; it focuses on providing a comprehensive overview of the existing ones as well as their results.
- **Study design:****
  - Narrative reviews.
  - Clinical study designs (RCTs, Cohort studies, case-control studies, cross-sectional studies).
  - Reviews or meta-analysis.
  - Non-peer-reviewed sources.
  - In vitro and In-vivo studies.
- **Language:** No restrictions.
- **Article specifications:****
  - No access to full text or incomplete data.
  - Studies with unclear or incomplete methodology.
  - Non-peer-reviewed publications.

Background/Rationale

1 Breast cancer (BC) is the most frequently diagnosed cancer in women worldwide, with 2 million new cases diagnosed each year. Most breast cancer cases are sporadic. However, it is estimated that 5-10% of cases are due to genetic susceptibility. This vulnerability is majorly due to various mutations in the two tumour suppressor genes BRCA1 and BRCA2. In fact, women who inherited and carry these mutations are more at risk of developing the disease when compared with the general population.
The BRCA1 and BRCA2 genes are tumor suppressor genes involved in DNA repair, by regulating the homologous recombination (HR). Currently, more than 1600 and 1800 mutations have been identified respectively in BRCA1 gene and BRCA2 gene. These genes are 83 and 86 kb long with coding sequences of 5.7 and 10.2 kb, scattered over 22 and 26 coding exons. Most of the mutations identified are point mutations and small insertions/deletions. Additionally, large genomic rearrangements have also been identified.
In silico approaches consist of studying these variants using computer modelling and/or computer simulation. It is still unclear how diverse these methods are and on what they are implemented. Our systematic review aims at providing a comprehensive overview of all the current in-silico approaches and studies performed on BRCA1 and BRCA2 variants as well as their results. In other words, our systematic review could help researchers gain an understanding of the current in-silico methods, procedures and methods as well as their respective results.

Objectives

2 Primary objective: Our systematic review aims to provide a comprehensive overview of all existing in silico approaches and studies conducted on BRCA1 and BRCA2 gene variants in breast cancer.
Secondary objective: To outline future perspectives and emerging trends in the field.
What are the different in silico methods used for studying BRCA1 and BRCA2 variants in breast cancer?
What are the different research areas covered by these studies.
What are the emerging in-silico methods currently under development for studying BRCA1 and BRCA2 variants in breast cancer?

Search Query

3 Pubmed: (((BRCA1) AND (BRCA2)) AND (MUTATION)) AND (IN SILICO)) AND (BREAST CANCER).
Scopus: (((BRCA1) AND (BRCA2)) AND (MUTATION)) AND (IN SILICO)) AND (BREAST CANCER).

Protocol references

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