BRCA Testing in Ovarian cancer Arabic Approach

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PARSGO

The Pan-Arabian Research Society of Gynecological Oncology

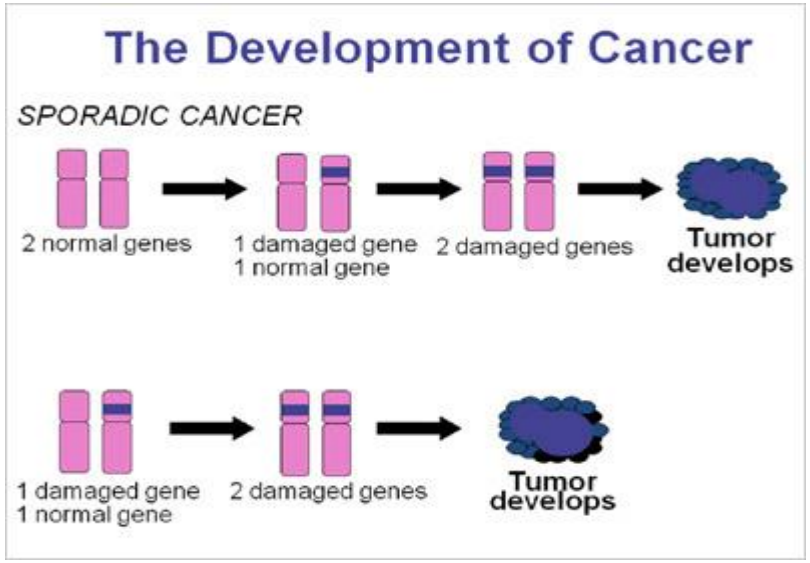
GYNECOLOGIC CANCER INTERGROUP

An Organization of International Cooperative Groups for Clinical Trials in Gynecologic Cancers

Know:BRCA

KNOWING YOUR BRCA GENE MUTATION RISK CAN SAVE YOUR LIFE

Development of cancer



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  Generally confer a modest increase in risk such as 2x

  Not attributable to a defect in a single gene, but rather to a combination of genetic alterations known as SNP‘s (single nucleotide polymorphisms)

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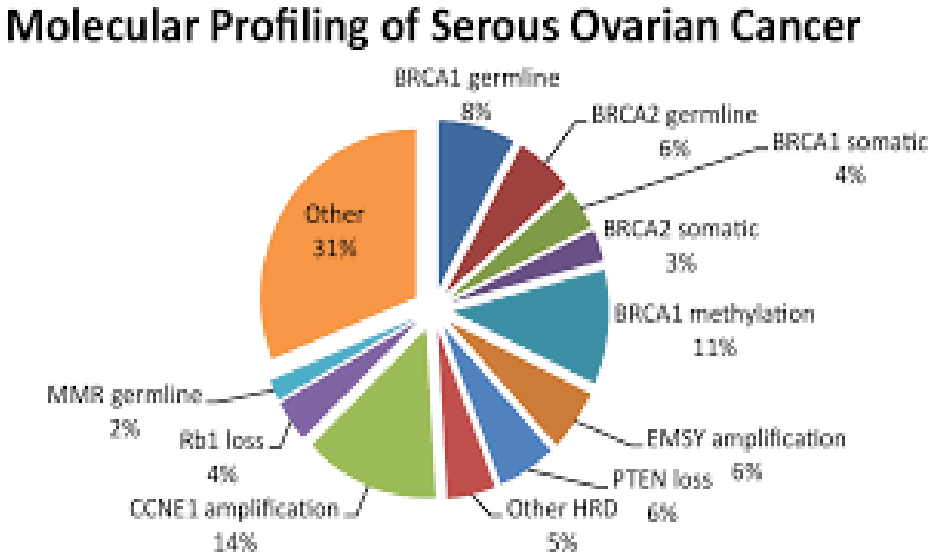
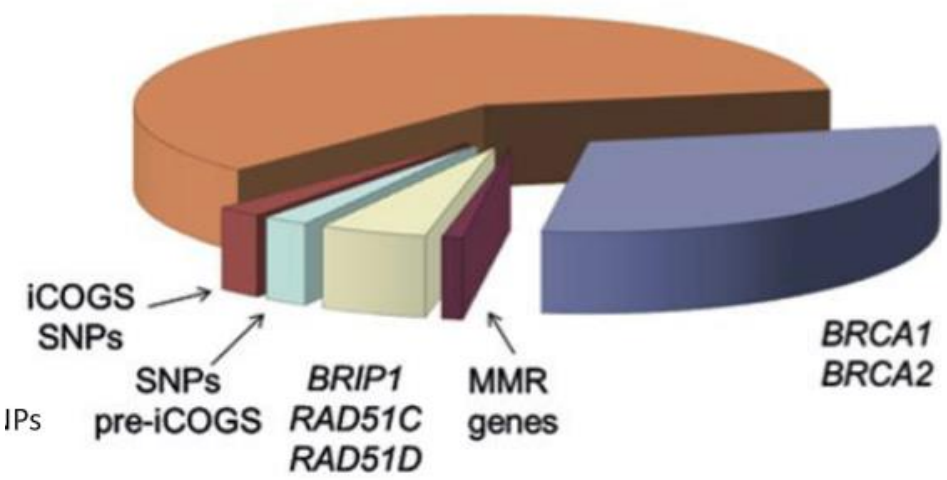


Goodman et al 2014

Germline mutations in ovarian cancer



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- **15%** in *BRCA1* or *BRCA2*
- **3%** in *BRIP1, RAD51C, RAD51D, PALB2, BARD1*
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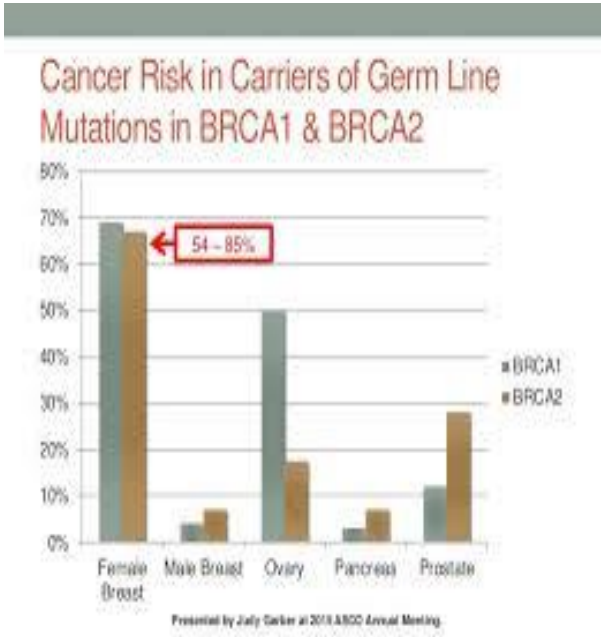
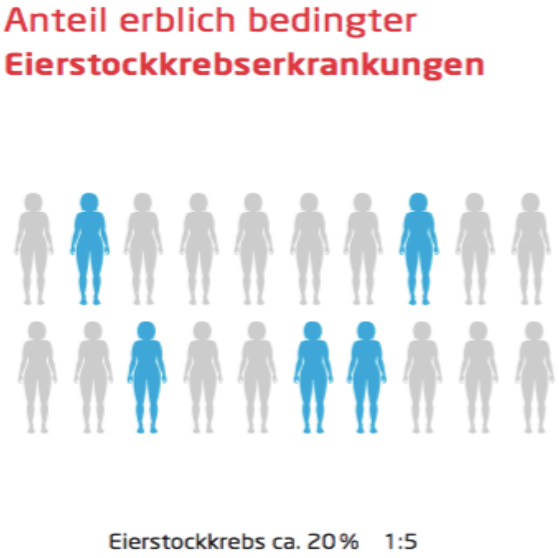
(GOG 218, GOG 262)
Norquist, JAMA 2016

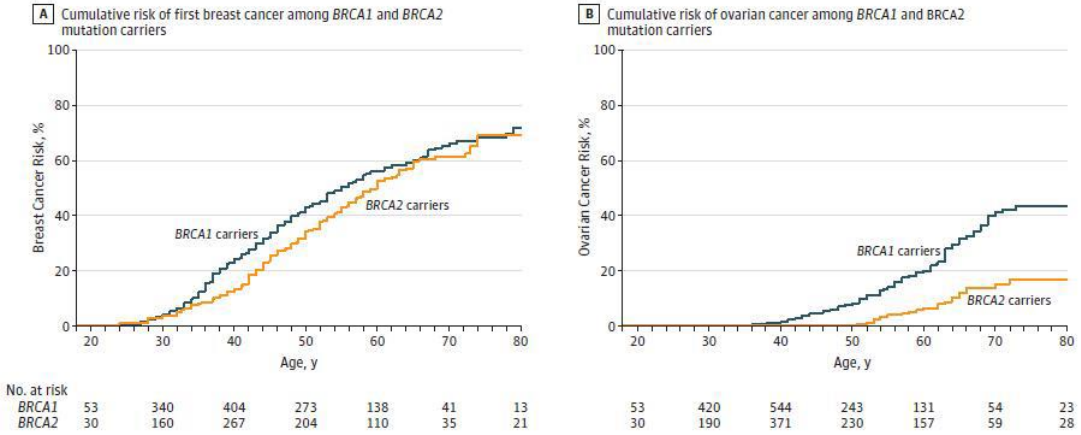
Cancer Risk in Carriers





Estimated Cumulative Risks of Breast and Ovarian Cancer in Mutation Carriers

- OVCA: Peak incidence
- BRCA1: 41-70y, BRCA2: 51-70y



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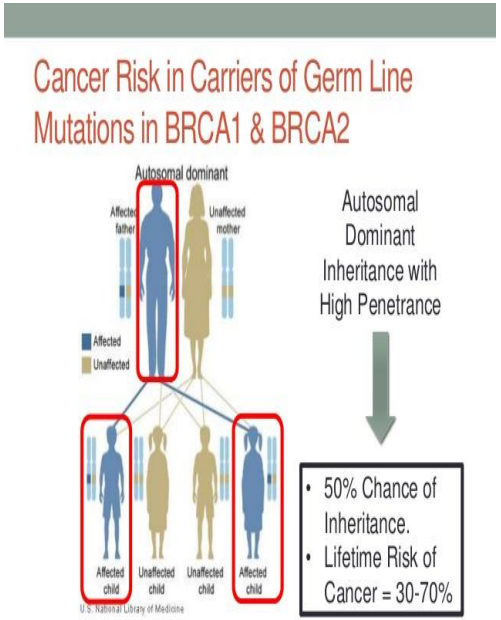
- Women and men equally affected
- 50% chance of inheriting mutation
- Vertical transmission
- Most mutations lead to truncated proteins



Function of BRCA1

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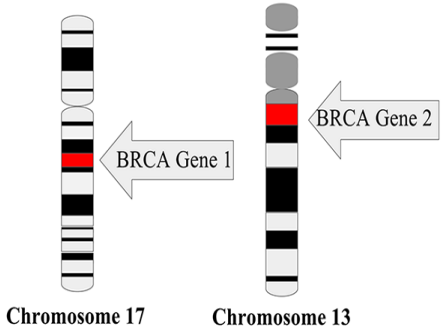

Yang, JAMA 2017

Function of BRCA2

- Regulation of RAD51 protein
- RAD51 required for double-strand
- break repair by homologous
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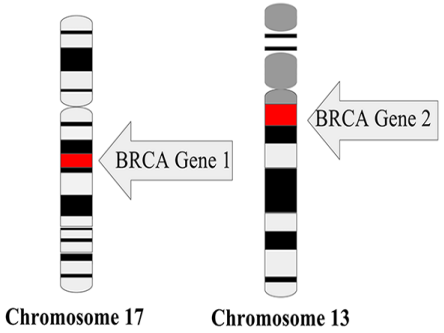

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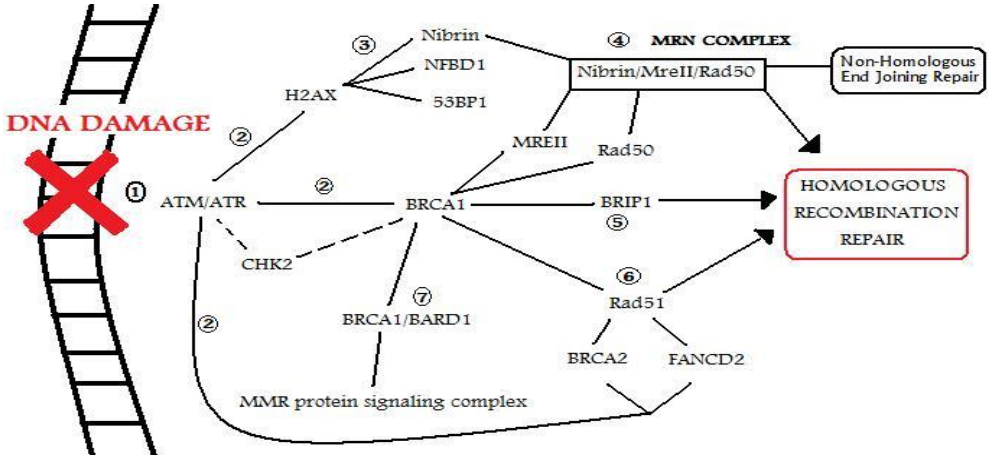
Function BRCA1/BRCA2



Prevalence of BRCA1/2 mutations

- General US population 1:400

- Ashkenazi Jews:

  - 1:40 - 1:50

  - 3 Founder mutations in 90% (BRCA1185delAG, 5382insC, BRCA2 6174delT)

- > 2000 different mutations

Roa 1996, Kauff 2002, McClain 2005, Saslow 2007

Purpose for Genetic Testing in Oncology

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How Many Cancer patients should Undergo Genetic Testing?

- When current NCCN guidelines are applied to large groups of cancer patients, the following approximate percentage of patients will be appropriate for genetic testing:

• Ovarian	100%	NCCN2008
• Breast	>30%	NCCN2018
• Colorectal	>25%	NCCN2015
• Endometrial	>70%	NCCN2015
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„Automatics“ FOR BRCA Testing

- Breast cancer by age 45 (invasive or DCIS)
- ANY epithelial OVCA, regardless of age or family history
- ANY male breast cancer
- Triple negative breast cancer by age 60
- Breast cancer in jewish. Woman
- Metastatic HER2-neg breast cancer (NCCN2018)
- Famils history of BRCA cancer (3 cancers within 3 degrees)
- First degree family members of any of the above

Arab

- The linguistic approach is a relaxed definition and it includes all populations speaking the Arabic language and living in a vast area extending from south of Iran in the east to Morocco in the west including parts in the south-east of Asia Minor, East, and West Africa.

- The political definition of Arabs is more conservative as it only includes those populations residing in 23 Arab States, namely: Algeria, Bahrain, Comoros, Djibouti, Egypt, Eritrea, Iraq, Jordan, Kuwait, Lebanon, Libya, Mauritania, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates (UAE), and Yemen.

Arab gene geography

- Genetic disorders are not equally distributed over the geography of the Arab region
- Nearly, one-third of the genetic disorders in Arabs result from congenital malformations and chromosomal abnormalities
- High fertility rates together. Consanguineous marriages, increase the rates of genetic and congenital abnormalities
- approximately 35% of genetic diseases in Arabs do not have a defined molecular etiology

Ghazi et al , glo card sci prac 2014

BRCA in arab world

- the proportion of BRCA1 and BRCA2 mutations could be higher in Arab women
- In Morocco, a large number of distinct polymorphisms and unclassified variants in BRCA2 , BRCA1 were described for the first time
- In Algerian women, four of 11 familial cases were associated with BRCA1 alterations
- In Tunisia, the prevalence of breast cancer is calculated to be between 16% and 38%. There, four novel unclassified BRCA1 mutations have been identified

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BRCA in arab world

- In Lebanon 38 BRCA1 sequence variants, many of which are novel were revealed

- Other unclassified BRCA1 variants, p.Phe486Leu and p.Asn550His, were detected in Saudi patients.

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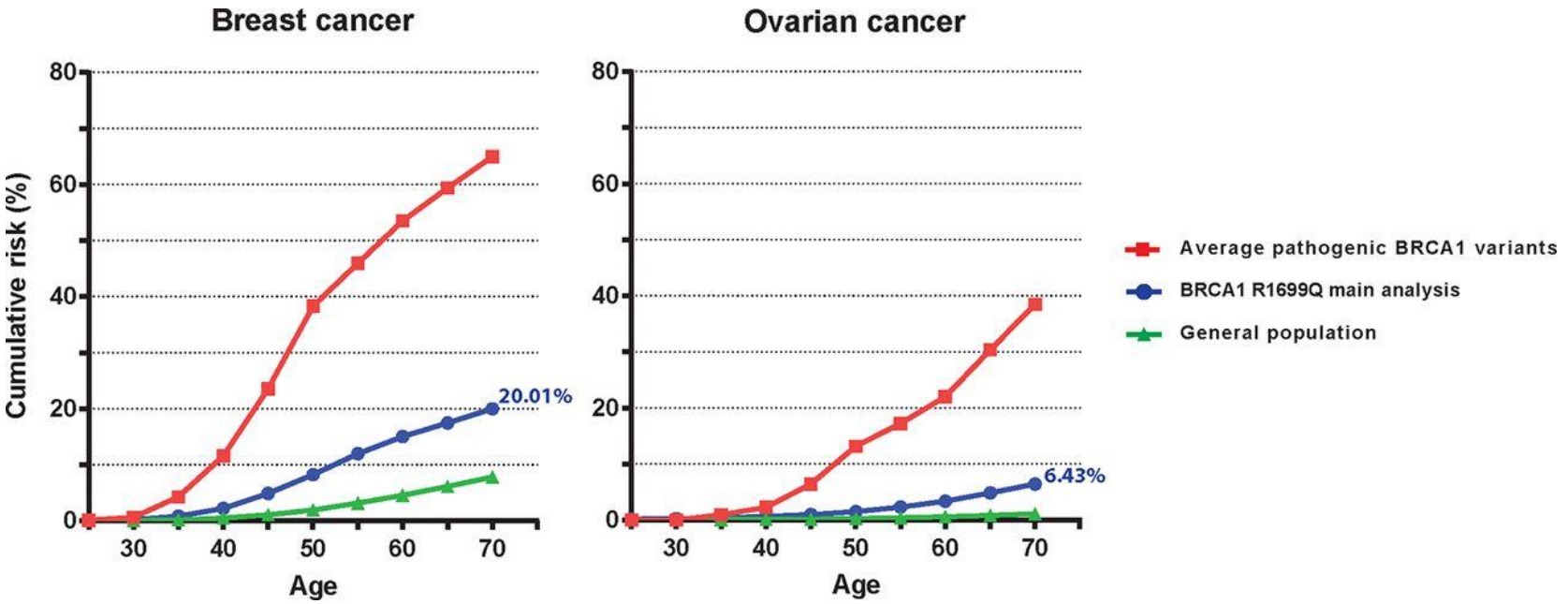
Cumultive Cancer Risk in BRCA1



Tools

- Implementation of simple questionnaire to personal and family cancer history

Testing procedure

- Blood sample of 5-10 ml (EDTA tube),DNA extracted from white blood cells

- Time till getting the result: 2 weeks

- Expenses:
  - Complete gene analysis: 3300 Euro
  - Carrier testing: 330 Euro

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Thank you

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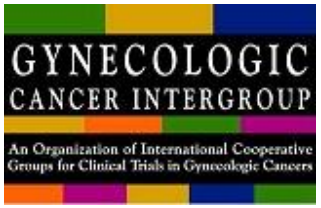

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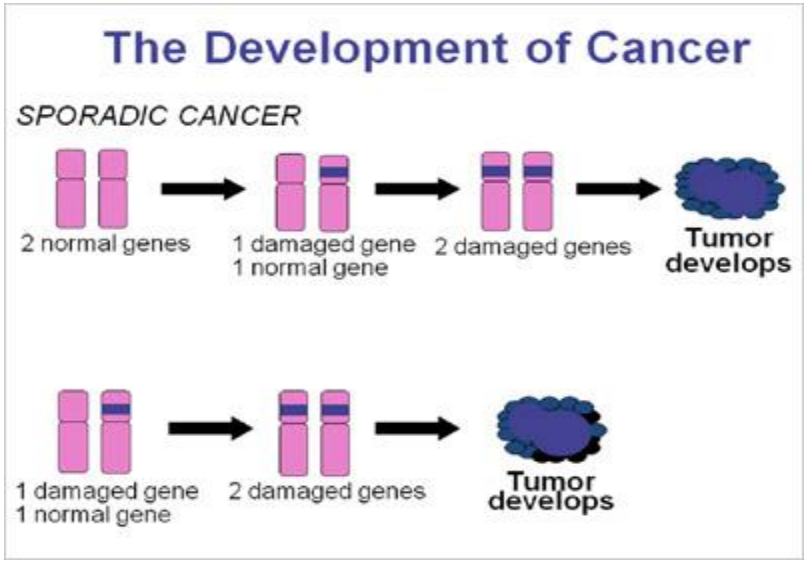

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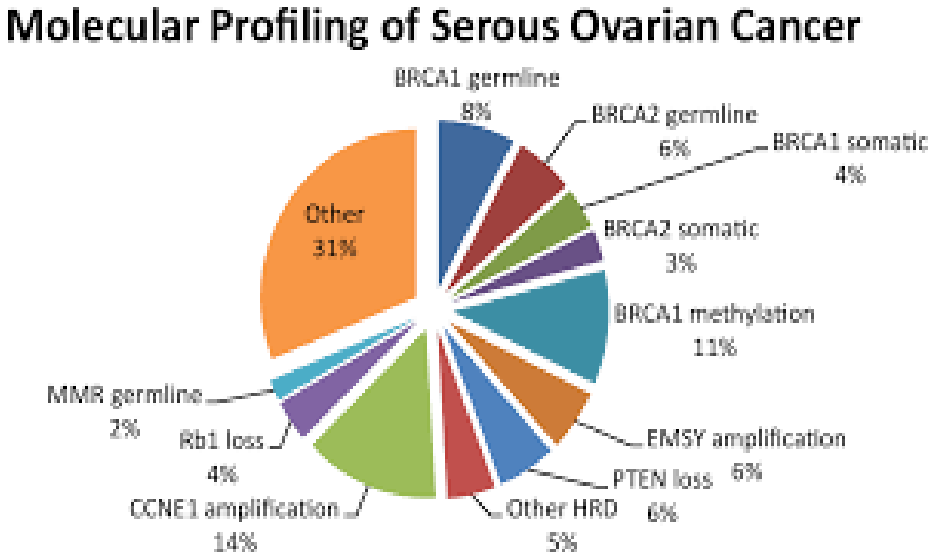

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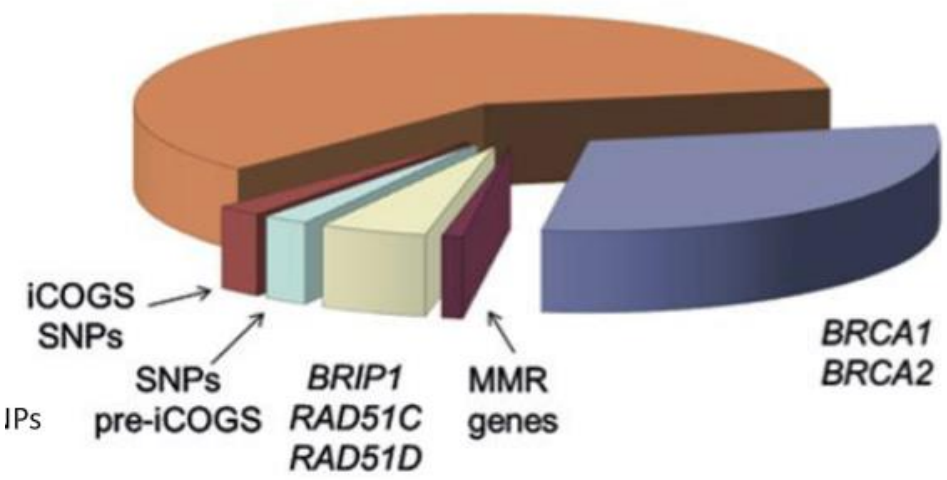

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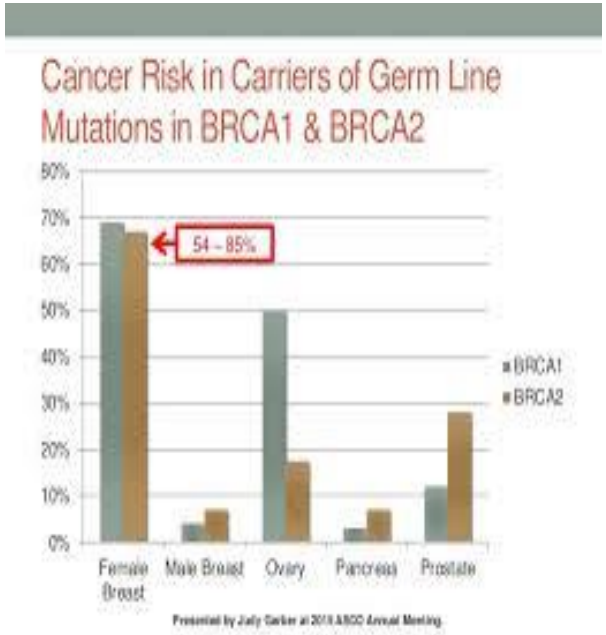
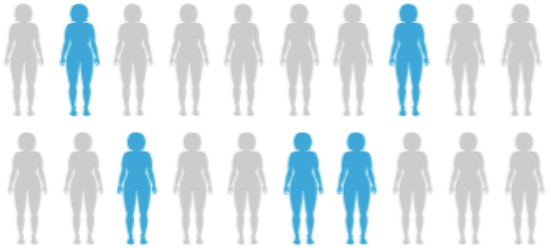


Anteil erblich bedingter
Eierstockkrebserkrankungen



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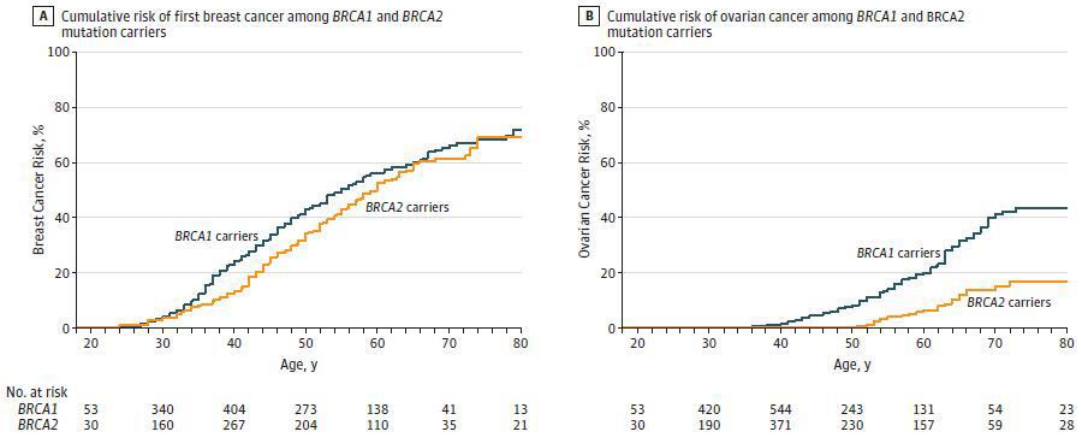

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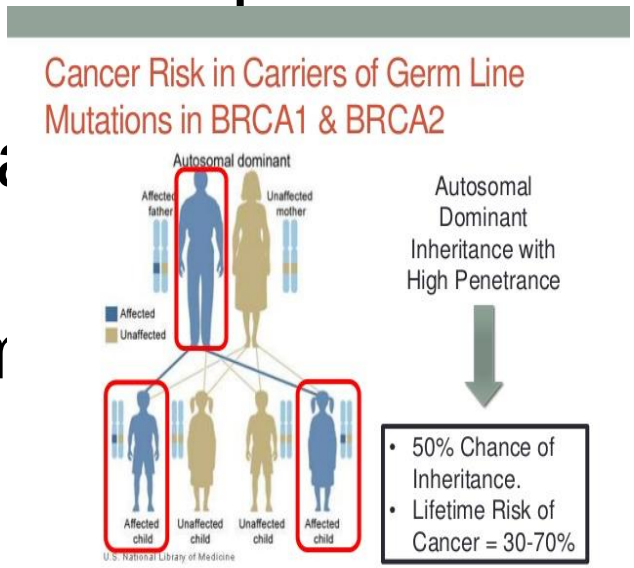

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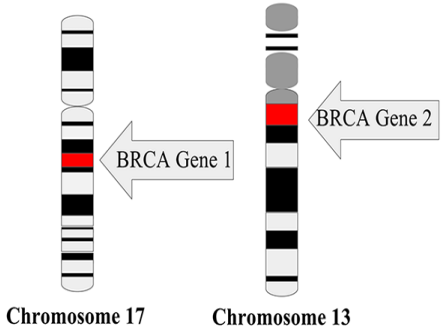

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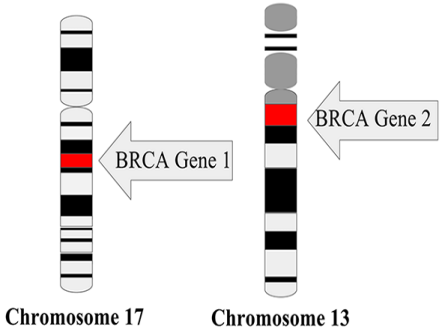

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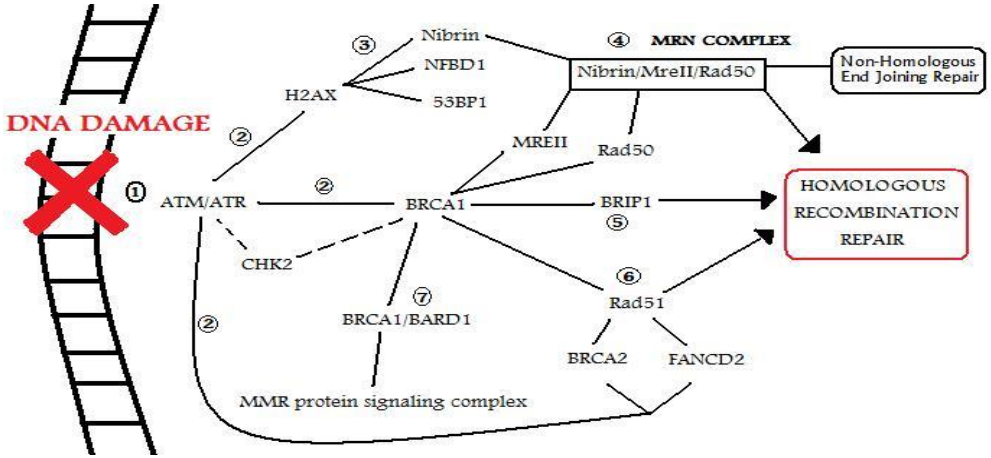

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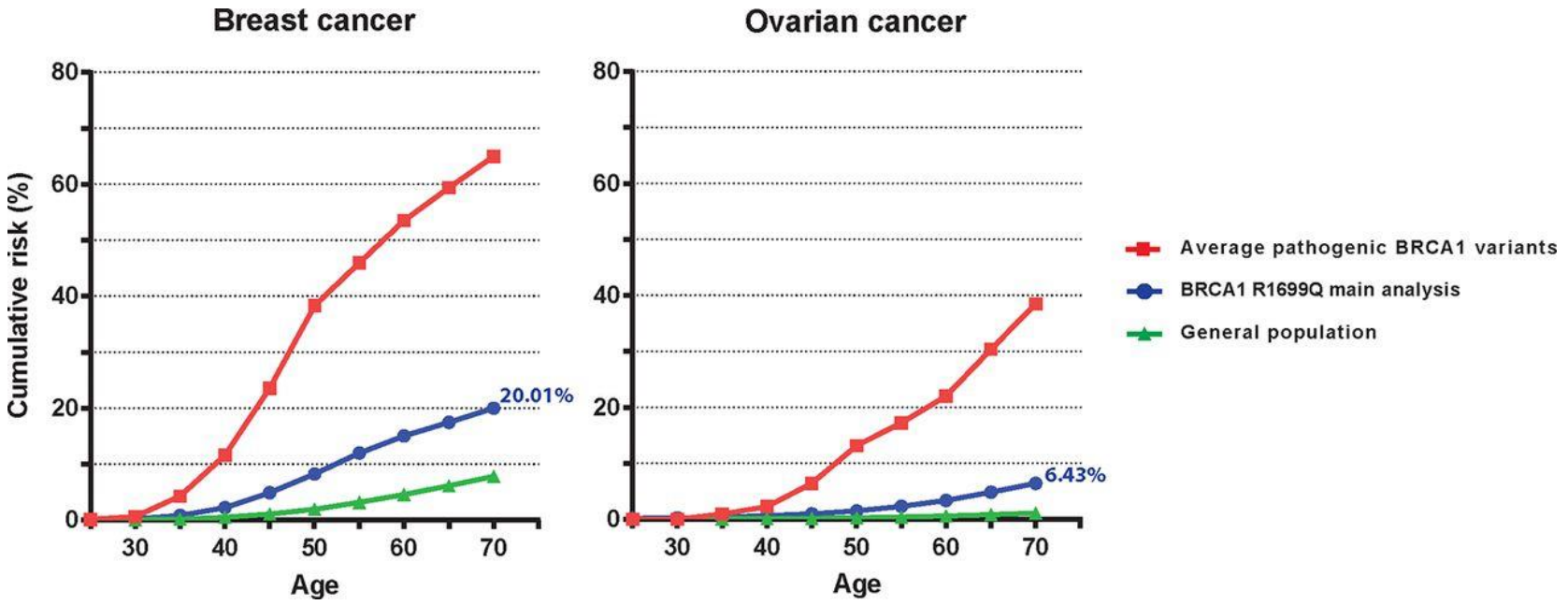

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